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CINEPLASTIC AMPUTATION

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FITTING physically handicapped persons into our social and economic structure has become one of the most vital problems of our speed machine age. These disabled persons, the human waste of our foundries, textile mills and transportation systems, must be rehabilitated or become a permanent burden to the community. Each day traffic and industrial accidents result in permanent maiming, or loss of limb. Disease and congenital deformity add their toll.

The man in the street is familiar with the physically handicapped individual who has overcome his disability and has made himself self-supporting and independent. He is not familiar, however, with the larger number who are unable to adjust themselves either because they cannot secure work or they cannot perform work.

Society must make a choice of either assuming full financial burden of relief or asylum for these individuals or else assist or train them in remunerative occupations in order to make them self-respecting and self-supporting individuals.

The goal of rehabilitation is the improvement of the mental and physical powers of the disabled person in order to meet the competition of those who are free from physical defects. By means of vocational training and physical restoration these powers can be improved, so as to enable the handicapped person to earn a livelihood.

Among those who require this rehabilitation service the amputation case is one that requires careful consideration. Employment is facilitated by providing these individuals with artificial appliances.

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The prosthesis serves to remove the psychologic aversion to the cripple by replacing his missing member, and offsets the economic prejudice of the employer by the increase in industrial efficiency of the amputee.

Because of the unsatisfactory experience with the ordinary mechanical arm, attention has been directed toward the development of a substitute arm in which the control can be achieved by natural muscular action.

In the cineplastic amputation the remaining muscles in the amputated stump are utilized to activate the prosthesis. By means of

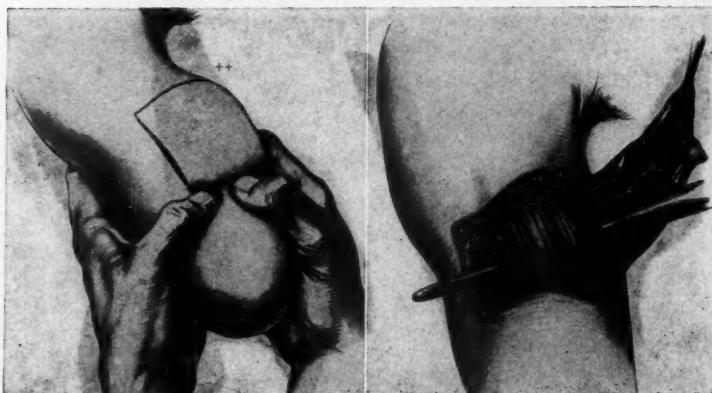


Fig. 1. Outline of tube flap.

Fig. 2. Elevation of skin flap.

pegs passed through canals in the muscles and attached to levers operating the artificial hand mechanism, the physiologic actions of the stump muscles are restored. The biceps and triceps muscles in the upper arm and the flexors and extensors of the lower arm control the grasp and release the fingers of the artificial hand.

The steps of the operation are as follows:

TECHNIC

While the patient is awake the muscle groups to be utilized for this operation are selected by having the patient contract the flexor and extensor muscles of the forearm. These are then outlined in methylene blue (See Fig. 1). The same outline is drawn on the volar side of the stump. The patient is then given a general anesthetic and the skin incised in the line of the outlined flap. The base of the flap is placed on the medial aspect of the stump since the circulation is richer at this point.

The incision is carried down to the muscle, forming a three sided flap of the skin and subcutaneous tissue. The entire operation is performed without a tourniquet in order to avoid any interference with the circulation of the flap.



Fig. 3. Preparation of skin tube.

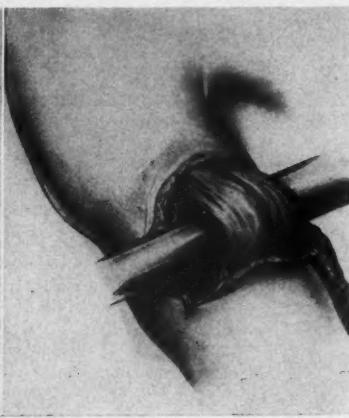


Fig. 4. Preparation of muscle canal.

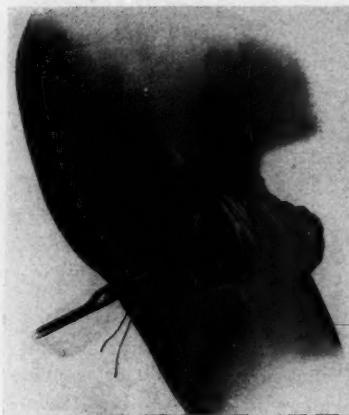


Fig. 5. Tube drawn through muscle canal.



Fig. 6. End of tube sutured to adjacent skin.

After bleeding is controlled the skin flap is raised from its underlying bed by blunt dissection (Fig. 2). The skin is undermined at the base of the flap in order to insure a flexible motor. The full thickness of the skin and subcutaneous tissue is utilized. The flap is then tested for any possible restriction.

The skin tube or loop is now prepared by reversing the flap and securing the end of the tube with a silk suture (Fig. 3). This is used both for traction as well as fixation. It is retained as a buried suture indefinitely or may be removed at the close of the operation.

The rest of the tube is approximated with subcuticular sutures of fine gut closely placed in order to insure perfect apposition. In this manner wide scars are avoided permitting friction of the peg which is to be later inserted in the

tube without irritation or ulceration. A probe is now passed through the tube to demonstrate its patency.

The tube is now retracted and the muscle prepared for canalization. Two parallel incisions are made in the muscle belly and an instrument passed through the muscle to form a canal.

It is important to use muscle and not tendon for the canal since the latter has no contractility. Movement of the canal depends on the alternate shortening and lengthening of the enclosed muscle as it contracts and relaxes.

The skin tube is now passed through the canal, holding the traction suture in the most superficial position in order to avoid distortion of the tube (Fig. 4). The edge of the tube is now sutured to the adjacent skin (Fig. 5). This leaves

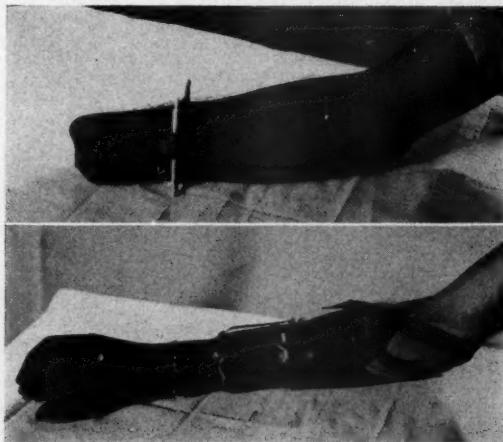


Fig. 7. Volar and dorsal motor in forearm stump.

Fig. 7a. With prosthesis.

a skin defect which must be closed. In young children, in the upper arm in adults and in those cases where there is a redundancy of skin in the amputation stump of the forearm, it is possible to close the defect by direct approximation of the skin edge. More frequently this cannot be accomplished without danger of skin necrosis. In this event the wound defect is covered with a Thiersch graft (Fig. 6). Zeroform gauze wicks are now inserted in the canals. The first dressing is done in about ten days, the pegs are inserted in about three weeks and the stump is ready for prosthesis in about six weeks.

More than forty years have elapsed since Vanghetti suggested the activation of prosthesis by utilizing the pull of muscles that remain in the amputation stump. Yet the cineplastic procedure has been regarded with indifference, apathy and even disfavor. While the early efforts of Ceci and Pellegrini were attended by indifferent results, Sauerbruch has demonstrated the validity of this method in over five hundred cases. In the Western Hemisphere, Bosch Arana alone showed a similar enthusiasm for this procedure.



Fig. 8. Double arm amputation. Double motor in left upper arm stump through biceps and triceps muscle. Right upper stump extremely short. Fixation canal used to fix apparatus to shoulder.

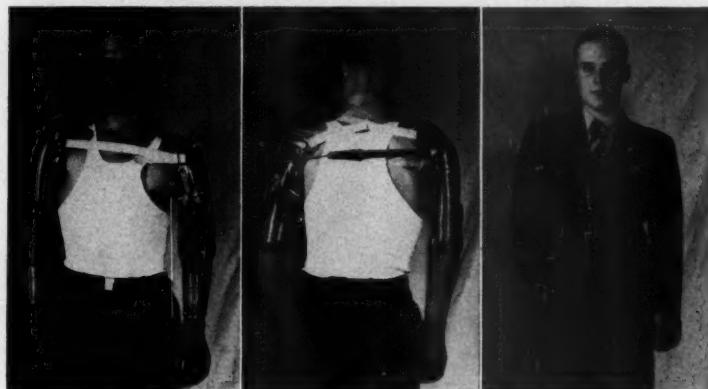


Fig. 8a. With prosthesis. Front view showing peg through biceps muscle.

Fig. 8b. With prosthesis. Back view showing peg through triceps.

Fig. 8c. Fully dressed.

Those difficulties that do arise can be ascribed to three factors: The patient, the operative procedure itself, and the prosthesis.

THE PATIENT

Unless the patient is cooperative, the best surgical result and the best type of prosthesis will be useless. The expectations of the amputee are frequently too great. He expects to duplicate the physiologic act of prehension with all its infinite variations. Even with ordinary mechanical arms, the individual is deceived by the unusual skill of the salesman. The latter, by dint of years of practice and



Fig. 9. Case of Construction-Gang Foreman with an upper arm stump. Front view.



Fig. 9b. Same as 9. Use of prosthesis in playing violin.

adaptation, has achieved an almost artistic perfection—one which the new amputee cannot accomplish in a short time. Discouraged by his lack of success, the limb is soon discarded.

The cineplastic arm has the advantage of depending on a natural physiologic process. The re-education occurs in a simple manner in a short space of time.

OPERATIVE PROCEDURE

The operation itself is quite simple. There are only a few points that need emphasis to avoid failure. It is most important to select the proper muscle or muscle group for canalization. It is impossible to tell beforehand just which muscles remain after the amputation. We depend, therefore, on the clinical test of visualizing the contraction of the muscles to be selected in response to the psycho-

physiologic act of opening and closing the hand at the site of amputation. The patient must, therefore, be awake and the muscles outlined with a skin dye just before the operation is undertaken.

The second important step, neglect of which has been responsible for many failures in the past, is to canalize the muscle and not the tendon. The latter has no contractility. The activation of the artificial hand mechanism depends on the movement of the peg which passes through the tube. This movement varies from $\frac{1}{4}$ to $\frac{1}{2}$ inch and is due to the alternate shortening and lengthening when the muscle contracts or relaxes.



Fig. 10a. Double forearm amputation with dorsal and volar motors in forearm.

Fig. 10b. Adjusting left prosthesis with right.

Fig. 10c. Smoking a cigarette.

PROSTHESIS

It is not difficult to manufacture the cineplastic arm. It is important that the weight of the apparatus be kept to a minimum. Furthermore, the mechanism should be as simple as possible. The more complicated the prosthesis, the less useful the arm. Theoretical advantages should be sacrificed for practical utility. For example, there is no need for incorporating a rotation mechanism at the wrist in forearm cases, since pronation and supination of the stump are still retained. However, in the upper arm amputation, this rotation mechanism is distinctly of value.

The arm can be designed for heavy as well as light duty, depending on the indications in the specific case. In the forearm amputation, no straps or apparatus are required above the elbow (Fig. 7). In the upper arm amputation, a strap to the opposite shoulder is necessary to secure flexion of the elbow (Fig. 8).

The results of this cineplastic amputation in a personal series of seventy-three cases are distinctly encouraging. Of this group, forty may be classified as highly successful. (See Figs. 9-11.) These individuals are consistently using the prosthesis at work and in the routine pursuits of life over a period of from two to six years.



Fig. 11. Two workingmen in Hair-Felt Factory. One forearm amputation, one upper arm amputation.

Of the remaining thirty-three, eighteen enjoy partial utility of their prosthesis. Unusual work requirements may render it impractical even to wear the arm at work, as in the case of one worker in a chemical plant who must immerse both arms in a solution as part of work operation.

Of the fifteen that can be classified as failures, five have been due to surgical complications. Infection of the skin tube, necrosis due to previous x-ray dermatitis, improper placement of canals, too short a stump for utilization of leverage of muscle motors and improper fit of prosthesis account for these failures. The remainder found it difficult to adjust themselves because of personality factors.

SUMMARY

The cineplastic amputation has distinct advantages over the ordinary mechanical prosthesis in that it employs natural physiologic methods in adaptation. The operative procedure is simple and the manufacture of the prosthesis is not complicated.

The most important factor is the proper selection of the patient and his psychologic preparation.

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NON-PENETRATING WOUNDS OF THE ABDOMEN

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INJURIES to the abdominal viscera caused by a non-penetrating blow constitute one of the most interesting and also one of the most serious conditions that we encounter in general surgery. The diagnosis of a penetrating wound of the abdomen is, of course, obvious, and these cases are usually operated upon without delay. However, we must recognize that any of the visceral injuries accompanying a penetrating wound may also accompany a non-penetrating wound. There may not even be the slightest bruise on the abdomen, and yet the injury may be of the most serious nature.

The abdominal viscera have slight protection against injury. The skin offers little support, because of its elasticity. The linea alba and the linea semilunaris are longitudinal areas, and are the points of least resistance. However, it is very seldom that force strikes parallel to these lines, because the majority of wounds are across the abdomen. The abdominal muscles and subcutaneous fat take the blow and sharp force is transformed into a dull, crushing force. The tone of the abdominal muscles has much to do with the protection of the viscera, and the better developed the muscles are the more protection there is against injury. The lumbar vertebrae are much closer to the abdominal wall than we usually think, and in children this distance may only be three or four centimeters. The solid organs, such as the kidney, liver, spleen and pancreas may be injured by either direct or indirect violence. The kidneys and liver have a good capsule and are also somewhat elastic—whereas the spleen has only a slight capsule. The spleen is also more granular and normally hangs from a pedicle, although it is often fixed by adhesions. This may explain the rupture of the spleen following comparatively light trauma, whereas injuries to the liver and kidney may be only slight following severe trauma. The intestines are most often injured by bursting due to hydraulic force and distention favors such injury. The intestine may be only bruised, and rarely may rupture later. The mesentery is in great danger of injury, resulting in severe hemorrhage—caused by an overstretching of the vessels.

One of the most interesting conditions which we encounter in abdominal injuries is a rupture of the deep epigastric artery. The condition is a rare one, but it should be borne in mind in the consideration of the trauma of the abdomen. It is usually associated

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with rupture of some of the fibers of the rectus abdominis muscle. These patients present signs and symptoms of intraperitoneal injury or disease. I have had six cases, five of which were operated upon. The patient who did not come to operation was a man 53 years of age. Twelve hours before admission he was seized with a rather severe pain just to the left of the umbilicus. The pain persisted. He gave no history of injury but stated the pain came on while resting. He was a thin man and did not appear ill. The physical examination was negative with the exception of a mass just to the left of the umbilicus. This was about 3 cm. in diameter, moderately firm and tender. His left rectus was fairly rigid, but otherwise the abdomen was relaxed. His bowels were open. The leukocyte count was 19,600 with 87 per cent polys. I adopted a conservative course. On the sixth day distinct ecchymosis was apparent, which extended down to his left inguinal region and to his suprapubic area. He ran a low fever. The leukocyte count fell to normal on the tenth day, when the mass had largely disappeared. He has had no trouble since. I have regarded this case as a spontaneous rupture of one of the branches of the left deep epigastric artery.

The others were all of traumatic origin, and all appeared on the right side, and there was no intraperitoneal injury in any case, although such had been my preoperative diagnosis.

Paralytic or adynamic ileus may follow any trauma to the abdominal wall. It may be the only condition present, or it may accompany other intra-abdominal injury. It is neurogenic in origin. Auscultation of the abdomen reveals no peristalsis, which tends to differentiate it from dynamic ileus. There is stasis of intestinal contents resulting from the absence of peristalsis. Nausea and vomiting may be an early symptom, but pain and tympanites are usually not present until later. This is of aid in differentiating it from mechanical obstruction where these symptoms appear early. The employment of the Levin tube for the continuous drainage of gastric and duodenal contents in this condition is essential, and is a marked advance not only here, but in postoperative ileus as well.

The liver is the most frequently injured internal organ. Its large size, composition and partial fixation render it susceptible to trauma. The capsule is usually torn, with varying degrees of parenchymal damage. Shock is the most common symptom, varying in its severity as a rule with the degree of damage. There is frequently much pain in the right upper quadrant and marked local tenderness and rigidity. Signs of internal hemorrhage derived from both clinical and laboratory evidence, occur early. There may be marked increase in liver dulness if the hemorrhage has been severe, although I have seen extensive damage and hemorrhage in which abnormal dulness

was not demonstrable. These cases should be operated upon as soon as possible since chance of recovery decreases steadily the longer the delay. The mortality ranges from 40 per cent within the first six hours to over double this figure at the end of twenty-four hours. It is advisable to have a donor on hand for blood transfusion before operation as there is no substitute for blood in these injuries. If a donor can not be secured autotransfusion should be performed if there is extensive hemorrhage. However, care should be taken to determine that there is no contamination from a rupture of a hollow viscus, or a large amount of extravasated bile. If there are fragments of liver tissue in the blood it should be filtered before using.

When the abdomen is opened, and the hemorrhage has ceased, the wound should not be disturbed if the edges are in approximation. If the wound is still bleeding the procedure of choice is to suture. If the bleeding is active it can be temporarily controlled by inserting the index finger into the foramen of Winslow, and then lifting up the free margin of the lesser omentum. The hepatic artery and portal vein may then be compressed between the thumb and index finger. The wound can thus be dealt with more easily since this gives temporary hemostasis. If suture is not possible or practical the wound should be packed, using a relatively small amount of gauze and not packing it with too much pressure; as it has been shown experimentally that much pressure about the liver produces obstructive symptoms. I believe all of these cases should have an abdominal drain since there is always some leakage of bile.

The spleen is a poorly protected organ and is frequently injured by slight falls, in which serious injury is not suspected at first. Often the patient seems to recover from the accident, only to develop symptoms of serious intra-abdominal injury several hours later. The chief signs are those of internal hemorrhage. Pain is usually present in the upper left quadrant, but I have had two cases of ruptured spleen that complained of lower right quadrant pain. Pain also may be referred to the left shoulder. Abdominal rigidity is usually present, more marked in the left upper quadrant. The area of splenic dulness may be increased, but I have found this to be a greatly over-stressed sign, and one not to be relied on at all. A rapid pulse and a continued lowering of the hemoglobin and the erythrocyte count are danger signals. Laparotomy should be performed as soon as the patient has recovered sufficiently from shock to permit an operation. Blood transfusion has no substitute in this condition. If a donor can not be obtained and there is much free blood, autotransfusion should be done. Where there is much damage the spleen should be removed. I have never sutured a torn

spleen. I have had fourteen cases of traumatic rupture of the spleen, with one death.

The use of thorotrust for the diagnosis of injuries to the liver and spleen has been advocated, but I do not subscribe to its use. I do not feel that there is ever sufficient clinical doubt in these cases to resort to the injection of this radioactive material, which remains in the body, and may do great harm.

The pancreas is probably more frequently injured than we realize, but fortunately severe damage is rare. A glycosuria during the convalescence of these patients may be the only symptom of pancreatic injury. I can recall only two severe traumatic cases of the pancreas, and in each case damage to another viscus was present; in one the liver was ruptured, and in the other I found a perforated intestine. The symptoms are those of profound shock and internal hemorrhage.

The kidneys are usually injured by blows in the flank, but may be injured by indirect violence. The treatment in these cases is governed by the condition of the patient and the extent of kidney damage. In the majority of cases the best treatment is that of conservatism, and immediate operation is indicated only where there is evidence of extensive injury or active bleeding. These injuries are extremely painful, and the patients are usually in varying degrees of shock when seen, and complain of pain on the affected side. Hematuria is present unless the ureter has been severed and this is an extremely rare condition. Rigidity over the affected area is usually present and the entire abdomen may be tender and rigid. If the condition of the patient warrants it a roentgenogram should be made. If this discloses a mass with obliteration of the psoas muscle shadow an excretory urogram should be done. Very careful attention should be paid to the quality and rate of the pulse and the trend of the blood pressure, and also to the hemoglobin and erythrocyte estimation. As long as these factors are satisfactory we should continue along conservative lines. A donor for blood transfusion should be on hand, and if operative interference proves necessary the patient should be transfused.

The bladder may be ruptured in severe pelvic injuries, or from a mild blow, either direct or indirect, if the bladder is full. Rupture may be extraperitoneal, intraperitoneal, or both. The symptoms depend on the location of the lesion, and the amount of damage done. The intraperitoneal rupture will give symptoms different from the extraperitoneal. In either case the symptoms are first those of shock. Local pain and tenderness in the lower abdomen are usually present, and there is a constant desire to void, which is per-

formed with difficulty. A few drops of bloody urine may be passed, and if the patient does not void he should be catheterized—which reveals blood. In extraperitoneal rupture a mass in the suprapubic region usually appears after a few hours, which does not disappear on catheterization. If the rupture is intraperitoneal the symptoms of peritonitis soon become manifest. Cystoscopy and cystograms are advocated by some as an aid in diagnosis; also, the injection of a measured amount of fluid to determine the amount which can be recovered, and to see whether the palpable mass increases in size. All of these factors may cause spread of infection, and I think should be used only where there is real doubt about the diagnosis. If employed they should be followed immediately by operation—if they reveal a positive finding. The treatment is, of course, surgical as soon as a diagnosis is established, and primary shock has passed. A donor for blood should be secured before operation as here again a blood transfusion has no substitute. On opening the peritoneum any fluid or blood is aspirated, and the bladder tear is repaired. Drainage should be instituted intra-abdominally and from the space of Retzius. If the injury is extraperitoneal the peritoneum should be closed before proceeding with the repair. The bladder is best placed at rest by free drainage through a suprapubic tube.

Rupture of the intestine is a potential injury following any severe abdominal trauma, and any person who has sustained a severe blow or trauma on the abdomen should be regarded with grave suspicion. The intestine may be torn completely in two, or the mesentery may be so badly damaged that gangrene of a considerable portion of intestine will develop. The intestine again may only be bruised, and perforation take place several days later. The literature on the subject seems to stress the fact that non-penetrating rupture of the intestine usually occurs at the fixed portions of the intestinal tract, such as the duodenojejunal junction, or at the ileocecal valve, or wherever it is fixed by adhesions. I have had twelve cases of traumatic non-penetrating rupture of the jejunum and ileum, but have never had a case that occurred at the above mentioned points. The cases in my experience have occurred in the free portions of the ileum and jejunum, and I have never seen a case where the intestine, anchored by adhesions, became the victim of traumatic perforation—though of course one can see how such a set-up would provide the proper mechanics.

The symptoms of intestinal injury may vary quite widely. Shock may be profound or almost absent. I have seen these patients walk some distance, and then insist there was no serious injury. If shock is profound the injury is probably extensive, with other organs involved. These patients complain of abdominal pain. The pain, how-

ever, differs from the pain in inflammatory perforation such as occurs in gastric and duodenal ulcers, where the patient can often tell the exact time of perforation. This type of pain in traumatic perforation is not met with, probably on account of the fact that the pain is not so readily noted due to the psychic excitement associated with the accident; then again, the non-inflamed peritoneum is not so sensitive. Tenderness and rigidity are very important and usually come on early. If the patient is not seen until five or six hours after the accident these findings are usually rather marked. Distention is not present as a rule until later, when the signs of peritonitis are becoming evident. Vomiting, when it occurs just after injury, has little significance, but is an important symptom if it comes on some time after injury. A steadily rising pulse rate after the initial shock has subsided is of significance. The temperature is often normal or only slightly elevated. The leukocyte count is usually elevated to 15,000 or 20,000 after the first few hours; but this is also the case in the presence of small intraperitoneal hemorrhage. However, I feel this increase in leukocytes is of distinct help. Obliteration of liver dulness I have found a very unreliable sign. An x-ray plate of the abdomen may reveal free air in the peritoneal cavity, and if there exists any doubt about the diagnosis I think this should be done.

I have had no case of traumatic rupture of the stomach from a non-penetrating wound.

I have had only one case of a rupture of the colon which might be classed as a non-penetrating wound. This involved a negro who had a high pressure air hose rammed into his rectum as a practical joke; it resulted in a most extensive perforation of the rectum and of the sigmoid, and there was no external evidence of injury.

CONCLUSION

An attempt has been made to present the more important types of non-penetrating wounds of the abdomen, with a general discussion as to their diagnosis and treatment.

DISEASE OF GALLBLADDER AND BILE DUCTS

Symptomatology and Results of Surgical Treatment

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THIS study is based on the clinical and follow-up records of 197 patients operated on for biliary disease at the Vicksburg Sanitarium and Crawford Street Hospital during the past ten years. It does not include malignant disease. The diagnosis was checked in a majority of cases and, in all that were chronic, by roentgenography, cholecystography and other diagnostic procedures not included in this discussion. The purpose is some appraisal of the value of symptomatology as an aid to correct diagnosis and prognosis, particularly in chronic gallbladder disease.

Aside from surgical mortality, the cause of poor results following biliary surgery for chronic complaints may be the extent of preoperative disease with damage to the liver, pancreas and bile ducts; but I do not believe this is true so frequently as claimed by some. Failure also occasionally follows incomplete surgery; for instance, failure to detect and remove calculi or to deal with other obstructions. Failure to obtain permanent relief of symptoms may be the result of recurrence of disease or the development of complications, such as duct stenosis. However, the group of surgical failures, that we should particularly like to avoid, is that which occurs in patients with chronic illness, whose preoperative symptoms were either caused by disease unrelated to the biliary tract or by non-surgical liver disease. This may be true of patients who have definite but symptomless gallbladder disease and with symptoms resulting from some other disorder. Avoiding surgical failures in such cases requires the use of all available diagnostic measures, none of which equals or in any way replaces careful clinical study.

Some of the most important diseases to be differentiated from chronic gallbladder are the following:

The nutritional disturbances called deficiency disease. These patients complain of digestive symptoms resembling those frequently attributed to the precalculous stage of cholecystitis. However, they are prone to be undernourished and to give a history of considerable weight loss. Weight loss in chronic cholecystitis is usually very moderate. Patients with deficiency disease often complain of sore mouth, of burning esophagus, and frequently have lienteric diarrhea. They

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often show a smooth tongue. Free hydrochloric acid is usually low or totally absent in the gastric contents. They have a tendency toward anemia. Some of these patients give a history of having had gallbladder operations without relief.

The anxiety state or psychoneurosis. These patients complain of any kind of digestive disturbance. They like to vomit immediately after eating. Aerophagia and belching are common. Marked weight loss is not infrequent. They frequently complain of mucous colitis. Insomnia is frequent. They too often have laparotomy scars.

CHART 1
197 OPERATED CASES GALLBLADDER AND DUCT DISEASE

Age Years	Cases	Operative Mortality	Per Cent
10 to 19.....	3	0	0
20 to 29.....	23	0	0
30 to 39.....	56	0	0
40 to 49.....	48	2	4.4
50 to 59.....	41	2	4.8
60 to 69.....	19	4	21
70 to 79.....	7	2	29
Total	197	10	5.07

Migraine sufferers often complain of digestive symptoms suggestive of biliary disease. Arthritis of the spine with pain from the lower intercostal nerves, the digestive disturbance of early pulmonary tuberculosis and syphilis of the central nervous system, may be confusing.

In dealing with acute illness diagnostic errors are probably less frequent. Acute gonorrhreal pelvic peritonitis occasionally extends to the liver region, giving rise to violent right upper abdominal pain very similar to that of acute cholecystitis, and this occurs at a time before the formation of a pelvic mass. Operation later will show characteristic violin-string adhesions extending downward from the liver edge and gallbladder region. Pneumonia with abdominal pain, coronary thrombosis, congestive heart failure with painful and tender liver, gastric crises of tabes and pain of lead colic can usually be differentiated by appropriate methods. Appendicitis and other acute surgical conditions of the abdomen are sometimes very difficult to differentiate from acute biliary disease, occasionally to such an extent that the diagnosis is only made at exploratory operation.

ANALYSIS OF RECORDS

AGE. Chart 1 shows the age, in groups, of 197 operative biliary cases along with operative mortality. The patients accounting for

the very high mortality in the higher age brackets were mostly those on whom cholecystostomy was done for very acute cholecystitis. In two of them the gallbladder had ruptured.

SEX. Chart 2 shows the usual preponderance of females. Only a small majority were parous.

CHART 2

197 OPERATED CASES GALLBLADDER AND DUCT DISEASE

	Cases	Per Cent	Per Cent Parous
Female	137	69	59
Male	60	31	

CHART 3

100 CASES OPERATED FOR GALLBLADDER OR DUCT DISEASE

	Per Cent
History of typhoid.....	24
History of appendicitis.....	32
Sedentary life	12
Ate heavily	39
Weight loss before operation.....	61
Arthritic pains	66
History of vague digestive symptoms.....	70
Feared discomfort or colic from full meal.....	72
Vomiting	50
History of jaundice	29
Dyspnoea with attacks.....	52
Fever with attacks.....	52
Chills with attacks.....	52
Epigastric pain	52
Right abdominal pain	36
Left abdominal pain	3
Low abdominal pain	3
No abdominal pain	6
Scapular radiation	60

Chart 3 was made up from the histories of 100 gallbladder and bile duct patients. This group was re-interviewed and the history carefully checked for accuracy. There was history of typhoid fever in 24 per cent. The incidence of typhoid in Mississippi in 1936 was .02 per cent. Culture of the gallbladder was positive for *Bacillus typhosus* in four of these cases.

There had been loss of weight before operation in 61 per cent. Weight loss was rapid and marked in patients with persistent common duct obstruction, amounting to from 20 to 80 pounds. Some

patients with common duct stones did not have persistent obstruction and showed correspondingly less weight loss. Patients with disease confined to the gallbladder usually showed only moderate weight loss, and this was true in the presence of long-standing disease.

Sixty-six per cent had complained of arthritic pains. The amount of relief from arthritic pains following operations did not suggest action of the gallbladder as a focus of infection.

Sour stomach, abdominal gas, belching and other indefinite digestive symptoms were commonly present; but, because the same symptoms are more often present in other disorders, they do not seem important as evidence of biliary disease. A history of abdominal pain or colic, though not always present, appears to be the most

CHART 4
178 PATIENTS WITH CHOLECYSTITIS

History of:	With Stones 100 Cases	Without Stones 78 Cases
Vague digestive symptoms	68%	66 or 84%
Feared full meal	70%	53 or 68%
Vomiting	48%	36 or 46%
Epigastric pain	55%	42 or 53%
Right abdominal pain.....	42%	34 or 43%
Scapular or back radiation.....	60%	42 or 54%
Jaundice	31%	15 or 19%

dependable of all subjective evidence. The attacks were usually irregular and, if the obstruction was not persistent or infection did not result, the patient usually felt well between the attacks. Over half of the patients feared a full meal, especially a heavy evening meal. The time said to elapse between eating a heavy meal and occurrence of discomfort varied from a few minutes to six hours. One patient gave a history of chill and high fever occurring about one hour after every full meal he had eaten for a period of two months. Not believing his story, I had him admitted to the hospital and required him to eat a full meal. This was followed, after a little more than an hour, by a severe chill and temperature of 104° F. Although he had no pain or jaundice, the diagnosis proved to be a common duct stone and its removal resulted in complete relief.

Pain was most often in the epigastrium. There was a higher incidence of epigastric pain and vomiting in common duct disease than in gallbladder disease.

Scapular and back radiation are tabulated together. Radiation to the back was more frequent in common duct disease. Jaundice

frequently accompanied acute cholecystitis without evidence of common duct lesion.

CHART 5
19 CASES CHOLEDOCHOLITHIASIS

History of vague digestive symptoms	9 or 47%
Epigastric pain	14 or 73%
Radiation to back	11 or 68%
Feared full meal	12 or 63%
Had no pain	4 or 21%
Fever without chills	4 or 21%
Chills and fever	11 or 58%
Jaundice	14 or 73%
Marked weight loss	15 or 79%
Vomiting	16 or 84%

RESULTS OF OPERATION

CHART 6

Results :	With Stones 100 Cases	Without Stones 78 Cases
Residual digestive symptoms	15%	30 or 38%
Recurrent colic	5%	4 or 5%
Complete relief	45%	15 or 19%
Improved	37%	51 or 65%
Unimproved	3%	11 or 14%
Died	7%	1 or 1.2%

CHART 7

Choledocholithiasis

19 Cases

Results :		
Residual digestive symptoms	3 or	16%
Recurrent colic	1 or	5%
Complete relief	14 or	74%
Improved	3 or	16%
Unimproved	0	
Died	2 or	10.5%

The symptoms of patients with calculous and with stoneless gallbladders (Chart 4), according to their stories, showed remarkably little difference; but it is hard to believe that the colic of chronic cholecystitis without stones is often as severe as that resulting from gallstones. At operation a few of the stoneless group showed advanced pathologic changes, both acute and chronic, and culture showed pathogenic organisms in some. One without stones was positive for *Bacillus typhosus*. Tissue pathology was generally much more advanced in calculous disease. Pathologic changes in stoneless gallbladders varied from marked inflammatory to very slight and 4 per cent showed no pathologic change.

Most patients with common duct stones (Chart 5) showed pain, jaundice, chills, fever, vomiting and wasting. However, some failed to show the most important symptoms. Twenty-one per cent gave a history of no pain and 27 per cent of no jaundice.

Clinical Results (Charts 6 and 7). Of symptoms persisting after operation, the vague digestive type was most frequent, 15 per cent in the cholelithiasis group, 38 per cent in patients without stone and in only 16 per cent of those with stone in the common duct. In recording recurrent colic patients who had attacks during a brief postoperative period only were not included. The average operative mortality for all patients was 5.07 per cent. Operative risk was low in patients with slight disease and high in those with advanced pathologic changes.

If the number of patients reporting complete relief is combined with those reporting improved, results were good in 82 per cent with calculous gallbladder, 84 per cent with stoneless gallbladder and 90 per cent of the common duct cases. But, judging by the number obtaining complete relief and the number of unimproved patients in each group, the common duct patients would appear the most satisfactory and the stoneless cholecystitis patients the least.

CONCLUSIONS

Vague and persistent digestive symptoms apparently do not constitute dependable evidence of surgical biliary disease.

Patients with demonstrated gallbladder disease may not expect relief by surgical treatment unless the symptoms are dependent on the biliary lesion.

Upper abdominal pain, occurring in irregular and intermittent attacks, though occasionally absent, appears to be the most valuable subjective evidence of surgical biliary disease.

Results in this series suggest that, aside from surgical mortality, patients with advanced disease fare better than those with only slight disorder. This may be true to some extent; but it may also indicate that diagnosis is easier and more often correct in the presence of advanced anatomic pathology, giving better results because of more properly directed therapy.

PRONTOSIL AND SULFANILAMIDE IN THE TREATMENT OF GAS GANGRENE

Report of Two Cases

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GAS gangrene was prevalent during the World War. Since that time due to the growing number of automobile accidents, it has appeared with increasing frequency in the civilian hospitals, so that now a surgeon working in a large city hospital is called upon to treat many of these infections.

In treating gas gangrene it has been our custom in the Grady Hospital to use mixed Anti-Tetanus Serum in all cases, amputating in some, in others opening the wounds wide and treating with wet dressings of Dakin's Solution.

While our results appear on a par with those of others, we have longed for better success. Recently we have added to our treatment prontosil and sulfanilamide with apparent improvement. We therefore wish to report the two following cases.

REPORT OF CASES

CASE 1.—About two hours after he had been accidentally shot while bird hunting on Feb. 14, 1938, T. C. C., a white man of 55, was admitted to the surgical service with a gunshot wound of the upper left thigh.

Physical examination revealed a gaping gunshot wound on the anterior surface of the left thigh just below the femoral triangle, and another on the posterolateral aspect, about half way down the thigh. The wound was very ragged and revealed much traumatized muscle. He was given one ampoule of mixed A. T. S. on admission, and the laceration was debrided. The dressing was kept moist with metaphen solution.

In spite of three additional ampoules of mixed A. T. S., the day after admission a gas gangrene infection developed in the wound with the typical odor. The culture from the laceration was positive for *B. Welchii*. There was crepitation over the entire thigh and over the lower anterior abdominal wall. His temperature ranged around 103 and his pulse rate ranged around 144. The left thigh was laid wide open by three radial incisions which extended down through the fascia, the muscles being separated. The incisions extended down to the muscles of the lower anterior abdominal wall. The dressing was then kept moist with Dakin's solution. He was given prontosil 20 c.c. every four hours for six doses and sulfanilamide gr. xx every four hours for two days. The temperature and pulse rate began to drop twelve hours after the prontosil and sulfanilamide therapy was begun and he seemed to be much improved. He was given two transfusions of blood during the next few days. He was soon considered out of danger.

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Extensive sloughing of the muscles occurred in the wound so that the femur was exposed through most of its length. Finally on May 3 the wound was clean enough to permit a secondary closure and pinch grafts. Twelve days later, a second pinch graft was done. Fortunately the large vessels and nerves were not injured so that below the knee the leg was not affected. He was able to lift the leg in bed but, partly on account of atrophy of disuse, was not able to walk. Gradually epithelium covered the whole denuded surface (Fig. 1). He was dismissed from the hospital on June 8 in relatively good condition although not yet able to walk.



Fig. 1. The appearance of the thigh 3 months after injury and gas gangrene.
Note the pinch grafts. (Case 1.)

CASE 2.—B. C., a white man aged 28, was admitted on the orthopedic service on Feb. 20, 1938, with diagnosis of: (1) fracture of lower third of the left radius and ulna, (2) compound fracture of the first metacarpal, (3) deep laceration of the palm and wrist with severed flexor tendons, (4) chip fracture of the head of the second metacarpal, (5) fracture of the styloid process of the left ulna, (6) acute alcoholism. These injuries had been incurred in an automobile accident a few minutes before.

He was carried to the operating room on admission where the laceration was thoroughly debrided, and an ampoule of mixed A. T. S. administered. The A. T. S. was repeated the next morning. Two days after admission, gas gangrene with its typical odor developed. Culture from the wound was positive for *B. Welchii*. He had temperature of 103 and the pulse ranged from 140 to 150. The wound was laid wide open from the hand up to the mid-forearm with three radial incisions down through the fascia, separating the muscles. The wound was then treated with an arm basin of Dakin's solution. He was given 20 c.c. of prontosil intramuscularly every four hours for six doses and sulfanilamide gr. xx every four hours for five days. His temperature and pulse rate began to drop twelve hours after the prontosil and sulfanilamide therapy

was instituted and his general condition became much improved. On March 1, it was decided to do a guillotine amputation of the lower forearm because of the poor blood supply of the hand, which had become gangrenous. He stood the operation well. On April 8, the stump was refashioned with good results.

DISCUSSION

In the light of past experience, we estimated that the life of the first patient would be lost but were gratified that this did not occur and much beyond our expectations, his leg was saved.

In the second case, we anticipated at least a loss of his arm just below the shoulder but instead, most of the forearm was saved.

We are not sure that sulfanilamide was specific for the *B. Welchii* in these cases. It is possible that the drug acted only through destroying the streptococci that were also present, and thus made the gas bacillus more amenable to treatment.

In both cases soon after the prontosil and sulfanilamide were started, the progress of the infection was arrested and the patients began to improve. We cannot help but feel that these drugs played a strong part in the good results obtained in these two cases, and strongly recommend further trial of them in the treating of gas gangrene.

MODERN METHODS IN THE TREATMENT OF PYOGENIC INFECTIONS

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IT has long been an axiom of bacteriology that the occurrence of infectious disease is conditioned by the resistance of the host, the virulence of the bacteria and the number of the infecting organisms. It follows as a corollary that the treatment of an established infection should be designed to increase host resistance and to decrease the virulence and number of the infecting bacteria. This implies that the successful clinical management of infections is as much a problem of antibodies and bacterial variants as of poultices and surgical operations. The purpose of this discussion is to present a conception of pyogenic infection which is based upon the bacteriologic and clinical study of infected patients.

It is important to define certain terms and phrases at the outset of this discussion.

The *septic component* of an infection is attributable to the survival and growth of bacteria in the body. The antibody which is elaborated to aid in the destruction of these bacteria is an antibacterial antibody and reacts directly with chemical constituents of the organic structure of the organisms.

The *specific toxemic component* of an infection is attributable to a poison or toxin produced by the bacteria and different bacteria produce various poisons which give rise to diverse clinical signs. The antibody which neutralizes this poison is called an antitoxin to distinguish it from the antibacterial antibody. Antitoxins do not react with the constituent parts of bacterial bodies.

The *non-specific toxemic component* of infection is attributable to the absorption of the products of suppuration. This non-specific toxemia of suppuration produces a constant clinical picture regardless of the causative bacteria.

The methods of evaluating and controlling the severity of the infection, the virulence of the organism and the resistance of the

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host are best illustrated by reference to a single organism. The beta-hemolytic streptococcus is ideally suited to this discussion.

THE SEVERITY OF THE INFECTION

The severity of the infection is determined by an evaluation of the clinical picture in terms of the various components of the infection. Each of these components has characteristic physical signs.

The septic component of hemolytic streptococcus infection accounts for the swinging "picket fence" temperature and pulse rate, cellulitis, lymphangitis, non-suppurative tender enlargement of the lymph nodes, chills and bacteriemia. For all practical purposes a chill is evidence of bacterial invasion of the blood stream but bacteriemia may exist without a previous chill. Hence it is necessary to culture a sample of the blood in many cases to determine whether the infection has been checked in the lymphatics or whether it has invaded the blood stream. Quantitative cultures should be done routinely to reveal the number of bacteria in the blood.

The clinical picture of the early acute infection may be dominated by the specific toxemic component. The specific poison of the hemolytic streptococcus is the erythrogenic toxin which produces the familiar cutaneous erythema of scarlet fever and a sustained elevation of the temperature and pulse. This toxin also damages the adrenal cortex and renders other tissues more susceptible to bacterial invasion. The strains of streptococci which produce this toxin are not bacteriologically different from other streptococci. Patients vary in their susceptibility to this toxin and strains of streptococci vary in their ability to produce it. The red streak overlying an area of lymphangitis is identical with the red rash of scarlet fever. The difference between these two clinical manifestations is simply in the degree of the toxemia.

The non-specific toxemia of suppuration is a later manifestation of streptococcal infection. The clinical chart of a patient with a completely "walled off" inflammatory process shows a sustained elevation of the temperature and pulse with none of the "spiking" element so characteristic of the infection in its septic phase. The differential blood count shows a shift to the right with an absolute increase in the lymphocytes and a return of the eosinophils. The urine usually contains albumin without red blood cells. The optimal time for surgical drainage has arrived when all of these conditions have been fulfilled.

THE VIRULENCE OF THE ORGANISM

The virulence of the organism is evaluated most effectively by laboratory methods. It is now recognized that there are eleven

major groups of hemolytic streptococci and that one of these groups is responsible for the majority of human infections. This important group has about 27 different types in it just as there are 32 types of pneumococci. Each of these types has four variant forms distinguished by certain biologic characteristics. It is important to know what variant is present in a given infection because such knowledge makes it possible to predict the probable course of the disease. Two of the variants are virulent, one variant is of low virulence, and the last is completely avirulent. Special culture procedures make the recognition of the variant involved as simple as the identification of the streptococcus.

THE RESISTANCE OF THE HOST

The resistance of the host is determined by a clinical notation of the degree of inflammatory fixation present and by an immunologic titration of the antibacterial antibody content of the serum.

Inflammatory fixation may be defined as that process of lymphatic occlusion that occurs in an infected area. This closure of the lymphatic capillaries "fixes" the infection and prevents the spread of the bacteria through the lymphatics into the blood stream. The presence of complete fixation is clinically evidenced by pitting edema, induration and localized fluctuation. Abscess formation appears to be accelerated in an immune host but it is quite clear that abscess formation can occur in the absence of any recognizable immune bodies. Bacteriemia may arise from an area of complete inflammatory fixation only as a result of septic endophlebitis secondary to perivenous or intravenous suppuration.

There are many methods of estimating the antibacterial antibody content of a patient's serum but the phagocytic method is the only one that can be performed rapidly enough to be clinically useful. In this test 0.25 c.c. of the patient's defibrinated blood is mixed with streptococci in the completely encapsulated phase of growth and then rotated in a sealed tube at 37° C. for half an hour. A blood film is made and examined to determine the number of streptococci that have been phagocytized by the leukocytes. By this method it is possible to titrate roughly the amount of antibacterial antibody in the blood. Patients that are doing well usually develop antibody on the third to the fifth day of their disease.

The presence of a typical scarlatiniform rash may be taken as evidence of the absence of antitoxic immunity. If there is no rash present there is no necessity to inquire further into the presence or absence of antitoxin in the serum. Atypical rashes can be classified

as scarlatinal in origin if they can be blanched permanently by the intracutaneous injection of specific antitoxin (Schultz-Charlton test).

TREATMENT

This combination of clinical and laboratory studies permits the accurate evaluation of a patient with hemolytic streptococcus infection. All of the above data can be collected within eighteen hours of the time of entry of a patient into the hospital. The information so collected is useful in indicating the weak spots in the protective mechanisms of the body and in determining a therapeutic plan. There are well established methods to:

1. Accelerate the process of inflammatory fixation
2. Destroy the bacteria
3. Neutralize the specific toxin
4. Attenuate the virulence of the bacteria.

Inflammatory fixation is hastened by methods which promote lymphatic stasis and increase capillary permeability. Splints, hot poultices, and bodily rest are the methods of choice.

The only known way in which the body can destroy gram-positive cocci is the process of phagocytosis and intracellular digestion. Virulent streptococci must be prepared for phagocytosis by the action of type specific antibacterial antibody whereas avirulent organisms may be phagocytized and digested without previous preparation by such antibody. If virulent bacteria are present and the patient has no antibacterial antibody it is necessary to inject serum containing the desired antibody. Such serums are not commercially available and it is necessary to use immune serum from human donors to supply the antibacterial antibody. Immune serums are selected by the phagocytic method. Immunity of this sort is type specific and donors may be found to possess antibody for one strain of hemolytic streptococcus and not for any others. It is not necessary for a prospective donor to have a definite clinical history of streptococcal infection and there is no assurance that the survivor of a streptococcus infection will have the antibody to his organism as a result. It is always necessary to determine the antibody present in such human serum and to perform the test with the streptococcus isolated from the patient.

The scarlatinal toxemia may be treated by the administration of antitoxin. Commercial antitoxins of high potency are readily available but these antitoxins are prepared from horse serum and have the disadvantage of producing serum reactions. Such reactions are dangerous in streptococcal infections because there is apt to be a spread of infection at the time of a serum reaction. The serum from

convalescent human cases of scarlet fever contains this antitoxin in lower concentration than the commercial serums but has the great advantage of being relatively innocuous. There is general agreement that human antitoxin is clinically satisfactory but it must be remembered that antitoxin combats only the specific toxemic component of an infection and does not prevent a progression of the septic component.

It is my belief that sulfanilamide is useful in hemolytic streptococcus infection because the drug has two effects upon the bacteria. The first effect is one which slows down the rate of bacterial multiplication. The second effect is a physicochemical alteration of the organic structure of virulent organisms which produces an attenuation of virulence. Strains of streptococci vary in their susceptibility to this latter action of sulfanilamide so that only certain strains are rendered completely avirulent and some strains are only slightly affected. The point to be emphasized is the fact that clinical experience has demonstrated that sulfanilamide alone may be inadequate in a fairly high percentage of bacteremias. The analysis of the treated cases reveals that sulfanilamide and antibacterial antibody are more effective than either one alone and that certain cases require antibody in addition to sulfanilamide. The immunotransfusion method is still the only way of supplying antibody to these cases and has repeatedly demonstrated its clinical value.

I have attempted to point out to you methods of diagnostic analysis and the indications for therapeutic methods as they exist for the hemolytic streptococcus. Similar methods are available for other organisms. However, it must be recognized that all of these measures are designed merely to help the body to convert a generalized or spreading infection into a localized one. Abscesses are an inevitable consequence of treatment in many cases and may be life-endangering by virtue of their location in an inaccessible site in the body. Fluctuation indicates the presence of pus but it does not give any assurance that the bacteria in that pus are no longer capable of destroying the life of the patient. The simple drainage of an abscess is more skillfully undertaken by the surgeon who has a high regard for the barriers of inflammatory fixation, the virulence of the organism, and the immunity of the host.

In conclusion it cannot be said that these methods have solved the problems of the surgeon in the management of infections because we now have living patients that have survived a previously fatal disease. These survivors present problems of diagnosis and treatment which we have rarely encountered before and which serve as a perpetual challenge to surgeons everywhere.

ETIOLOGIC AND THERAPEUTIC ASPECTS OF BRONCHIECTASIS WITH CLINICAL OBSERVATIONS ON BRONCHIAL LAVAGE BY THE STITT METHOD

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ETIOLOGIC CONSIDERATIONS

CLINICAL and experimental investigations of the past decade have enlightened us considerably as to the etiology of bronchiectasis. From these reports we may glean certain facts.

First, it is possible that certain congenital malformations of the bronchial tree may exist. Marcy¹ minimizes these anomalies. He believes that most all cases originate in the first three years of life due to infection plus certain mechanical features. Nevertheless so called dry bronchiectasis is reported in both adults and children. However, 8 of 20 cases reported by Wall and Hoyle² had slight sputum. Bohrer³ mentions such a maldevelopment in an 18 months old baby. None of these cases has been personally encountered; nor have any well established cases become completely dry under any sort of treatment. Such patients may represent congenital abnormalities that are fortunate enough never to have become infected. They are probably unusual.

Weinberg's⁴ report was complete and instructive. The bronchi of rabbits were obstructed with sand burs. Clinical and pathologic observations were made at progressively longer periods of elapsed time. The sequence of events leading to the bronchiectasis seemed to be:

1. Retention of secretions making a highly fertile medium for bacterial growth.
2. Destructive action of the infection on the bronchial wall.
3. Atelectasis distal to the obstruction.
4. An increased difference between intrabronchial and extrabronchial pressure caused by the atelectasis with further dilatation.
5. Further destructive bacterial action due to the large reservoir for infected material.

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Weinberg also concludes that outside organisms are not necessary to the process. He differentiates the rapidly developing bronchiectasis of obstruction from the less severe and more slowly developing bronchiectasis due to infection per se.

Therefore bronchial obstruction would seem to be an important factor in severe bronchiectasis. Neglected foreign bodies are a common cause. Likewise an endobronchial growth may give a secondary bronchiectasis. I have verified by lung mapping the resulting bronchiectasis in both conditions.

Whether this bronchiectasis is congenital or acquired, the paranasal sinuses occupy a prominent place in current literature as primary sources of infection. If a factor, is the modus operandi by inhalation or by way of the lymphatics? Mullin³ believes both routes are operative.

McLaurin⁶ and Quinn and Meyer⁷ used lipiodol in the nose and demonstrated some hours later by x-ray the iodized oil in the lungs of the same patients. This argues for the inhalation route.

Clerf⁸ feels that every case of bilateral bronchiectasis should suggest nasal sinus infection. Conversely, he argues that unilateral cases are much more apt to follow pneumonia, lung abscess, or foreign body.

Of course one cannot be too dogmatic. Thus Quinn and Meyer⁷ reported five unilateral cases having a concomitant sinusitis; and nine bilateral cases without associated sinus disease. Marcy¹ points out that many pulmonary lesions antedate the sinusitis; and that there are a number of bronchiectatic patients with no sinus infection. Nevertheless, the frequency of associated sinus disease with bilateral bronchiectasis should always direct attention to the paranasal sinuses.

Hodge,⁹ in a recent comprehensive review of the whole subject, published some interesting work. He placed lipiodol in the tracheas of bronchiectatic patients and was able to show by subsequent roentgenograms that the iodized poppy-seed oil appeared in the nasopharynges in only 3 of 10 patients. He got similar findings using mild silver protein. In neither group was any opaque substance demonstrated in the nose. He concluded the soft palate was an efficient barrier during coughing. This work argues against the sinuses being secondarily infected.

Moersch, in discussing Hodge's paper, calls attention to the swelling of the mucosa and increase of secretion of a bronchial fistula following an acute infection of the upper respiratory tract. He feels this points to a close relationship between sinus infection and

bronchiectasis and further states that 50 per cent of the bronchiectatic patients operated on at the Mayo Clinic for complicating sinus disease felt that they had received benefit despite indifferent objective results.

A pertinent fact may properly be interpolated here. One of my own cases had a unilateral pansinusitis complicating a bilateral bronchiectasis. This finding points to the sinus infection as primary. If secondary why would one side be infected to the exclusion of the other? Sinus disease in bilateral bronchiectasis has been frequently observed in our clinic. Not so much attention has been paid to merely hyperplastic changes as shown by x-ray. However, it is felt that hyperplastic changes with frank suppuration are contributing pathologic factors. Particularly is this true if a frank empyema of the antrum or frontal is present as shown by observation and irrigation. In all but 4 of 13 cases of proven bilateral bronchiectasis frank hyperplastic changes with suppuration were demonstrated. In 3, hyperplastic changes in one or both antrums were present on x-ray examination. In one case there was no x-ray record of the sinuses but no clinical manifestation of sinus infection was present.

Six cases of unilateral bronchiectasis showed the following objective and subjective findings: 1. A complicating sinus infection in only one (hyperplasia with suppuration). 2. A definite history of onset following influenza in one. 3. In another, an indefinite history of bronchitis with an acute pulmonary flare-up following tonsillectomy under ether. 4. In the fourth patient, no predisposing history but that of an automobile accident. 5. A fifth patient whose bronchiectasis followed an acute right upper lobe suppuration. This healed under conservative management including bronchoscopy and phrenicectomy. Some months later he returned with a basal bronchiectasis on the same side. This would suggest that the gravitation of pus into the lower areas during the acute stage predisposed to the bronchiectasis which followed. 6. A sixth patient had a bronchial carcinoma, and a bronchiectasis secondary to the neoplastic obstruction.

Other etiologic factors must be considered. Thus Hodge⁹ also mentions the work of Anspach¹⁰ and Sippe¹¹. The former ventures the opinion that allergy or an acute pulmonary infection may give an initial obstruction by the swelling of the mucous membrane and the production of thick tenacious sputum. This would produce, particularly, a basal atelectasis with secondary bronchiectasis if not relieved.

On the other hand Sippe¹¹ believes that hypoglycemia and ketosis may be factors in production of both sinus disease and non-tubercu-

lous pulmonary fibrosis. His references to bronchiectasis are vague and indefinite. He reports nine cases and argues that an exudative process results because of inability to retain water in the tissues. The treatment is the administration of dextrose. I have had no personal experience with such patients.

Brown¹², one of Sippe's fellow countrymen, disagrees sharply with this theory. He believes that the hypoglycemia is much more apt to be the result of chronic infection than the cause of it.

Smith¹³ feels that fusospirochetal infection may be an important factor in the genesis of some bronchiectasis. Most other writers, however, discount any special infection as a primary etiologic consideration.

Epitomizing, then, a complicating sinus infection is common in bilateral bronchiectasis; only occasionally so in unilateral bronchiectasis. The sinus infection may be either a primary or a secondary factor. Bronchial obstruction is a potent causal factor regardless of the type of obstruction. Prolonged infection, particularly with incomplete drainage probably also contributes to some bronchiectasis. Congenital malformations may occur. These are probably rare. If they remain uninfected, they constitute so-called dry bronchiectasis; if infected secondarily they are not distinguishable from any other bronchiectasis. Lastly, other etiologic factors seem unimportant.

THERAPEUTIC CONSIDERATIONS

The frequency of sinus suppurations with bilateral bronchiectasis has been mentioned under etiology. Churchill¹⁴ feels that the sinuses should be treated but radical surgery deferred until after lobectomy. Marcy¹ holds there is little direct effect on the bronchiectasis by relief of the sinus disease but that the general health is improved and a source of infection removed. The latter view has influenced my policy until now, viz., radical sinus operations when indicated before undertaking active treatment of the bronchiectasis. On 7 of the 13 bilateral cases previously alluded to, bilateral radical antrum, ethmoid, and sphenoid operations were first done. An eighth patient, with a unilateral pansinusitis, had an external frontal, ethmoid, sphenoid, and radical antrum on the affected side before undertaking bronchial lavage. Let it be noted again, however, that I am stressing the cases with true suppuration and not merely hyperplastic changes. These latter, or silent cases, are still on more debatable ground.

By following this policy, allergic hyperplastic changes are not so apt to be confused with those due to chronic infection. However,

suppuration superimposed on allergy, sometimes demands surgical interference. It is interesting to note that none of the case records here discussed, whether unilateral or bilateral, exhibited any clinical evidence of allergy; nor was there a personal or family history of allergy.

Interest in other therapy has received great impetus since the advent of bronchoscopy, lung mapping, and modern thoracic surgery. The first may be classified as both diagnostic and therapeutic.

Surgery has been thought to be applicable only to the unilateral case. However, Churchill¹⁴ has reported 5 bilateral lobectomies with one death. These, of course, are done in two stages. He also reports a total pneumonectomy for bronchiectasis. His statistics show the remarkable progress of thoracic surgery: a mortality of 6.1 per cent in 49 patients; 2.6 per cent for 38 other patients; and the last 50 lobectomies without a death. Marcy¹ feels lobectomy is the surgical method of choice. With accumulating surgical reports of excellent therapeutic results, there now seems real hope for these previously hopelessly ill patients. Preliminary bronchoscopy or bronchial lavage, or both, may make a better surgical risk.

On many, whether the bronchiectasis is unilateral or bilateral, phrenic operations have been done. Usually the worst side is selected by choice. A few cases of bilateral phrenic have been reported¹⁵ but naturally this is a procedure to be approached with caution.

Personal experience has shown phrenic operations as a rule to be disappointing. Perhaps too much has been expected. I have seen only one dramatic result and that was in the bronchiectasis previously mentioned secondary to bronchial carcinoma proven by bronchoscopic biopsy. The man died later of his carcinomatosis but was rendered sputum and fever free. It proved valuable in repeated hemorrhage in one case. The side of hemorrhage was first determined bronchoscopically.

Similarly pneumothorax yields disappointing end results, even though maintained over a long period of time. Temporary benefit may ensue. Churchill¹⁴ mentions one such case collapsed for four years who has returned essentially to the previous condition. One of my patients first had a phrenic operation followed later by a pneumothorax on the affected side and maintained for 17 months. Lung mapping then showed residual multiple bronchiectatic cavities.

Prolonged postural drainage is equally discouraging. Bohrer³ refers to the work of Brown and Boyd of Toronto. A fixed inclined position for as long as 16 months in their pediatric clinic gave only temporary improvement.

Recently Berck and Harris¹⁶ reported their results with roentgen therapy. Three of my patients have since been treated by reputable x-ray men using their technic. All were advanced bilateral cases. One patient died shortly after the treatment of an acute pneumonic exacerbation with secondary right heart failure; one has received no benefit at all and returns occasionally for lavage for temporary relief; and one reported no appreciable change.

Radical surgery then would seem to be the only salvation for these patients and particularly the unilateral case. The bilateral bronchiectatic, less favorable surgically, deserves further consideration.

It is this group who merit real attention and further study. A diagnosis thus established, the physician has been apt to shrug his shoulders and look askance at the patient. Postural drainage and high caloric feedings were advised; perhaps a few bronchoscopies done; and arsenic given if indicated.

It is emphasized, arsenic is only an adjunct to other therapy. Smith^{18, 17} has done highly commendable work on fusospirochetal infection in bronchiectasis and pulmonary suppurations. Unfortunately, after his work many general men in our State seemed to get the impression that all that was necessary in these cases was the administration of arsenic. I am sure, after hearing and talking with Dr. Smith, that he did not mean to leave that impression. Certainly we are indebted to him for so ably re-emphasizing this factor. Nevertheless, in the advanced cases, as will be shown in the records that follow, every conservative weapon at our command must be utilized to get appreciable improvement without surgery.

As a result of Smith's work, I now do this: give arsenic for a few doses in a patient with a foul sputum even though the fusospirochetal organisms are not found on dark field examination of a bronchoscopically aspirated specimen. He pointed out in a personal conversation that there are three organisms that will give a foul odor: Welch bacillus, colon bacillus, and fusospirochetal infection. The first two would hardly be expected in the lung. Hence in such cases it is better to err on the side of safety, and use arsenic in connection with other therapeutic measures. A personal preference is for sulpharsphenamine intramuscularly because of greater safety over intravenous medication.

A bronchoscopic specimen of pus is desirable for examination for fusospirochetal infection. Moreover, stricture, neoplasm, unsuspected foreign body, and obstructing granulation tissue may be eliminated and dealt with by appropriate measures if present.

Lipiodol may be instilled at the time of bronchoscopy. This sometimes gives a very satisfactory lung mapping. My best plates have been obtained by placing a catheter in the trachea under cocaine anesthesia and injecting either side at will by changing the position of the patient. This is done in the x-ray room.

Any history of allergy should indicate preliminary skin testing with lipiodol. While it has not been done routinely, such a routine sensitization test would provide greater safety.

The diagnosis now established, is further bronchoscopic treatment indicated? The question is answered indirectly. A few bronchoscopic aspirations done once or twice weekly will help stabilize the patient by providing better drainage. Like any other therapy, its usefulness is limited in advanced cases. However, excellent results may be obtained at times in the early lesions of childhood. Ans-pach¹⁰ in his classic paper has pointed out that atelectasis often precedes the development of bronchiectasis. This is an indication par excellence for bronchoscopic aspiration. This prophylactic treatment cannot be emphasized too strongly. Personal satisfying experiences have been previously reported¹⁸ and these experiences confirm those of others of which time and space do not permit mention.

Three years ago, one of my confreres stimulated my interest in bronchial lavage by the method of Stitt. I corresponded with Dr. Stitt and have followed his technic with only one modification, viz., I had an adapter made to fit the catheter, and after lavaging with hypertonic salt solution, made according to Stitt's formula, I use a suction machine to cleanse further the lung before instilling 1:3000 merthiolate solution. Since Stitt¹⁰ has published the exact technic, it is hardly pertinent to review it in detail here.

Suffice it to say the whole procedure can be done in the office. One dram of elixir of alurate is given as preliminary medication to forestall any possible ill effects from cocaine. The pharynx and larynx are anesthetized with 20 per cent cocaine and then 4 per cent cocaine is dropped into the trachea by syringe. The catheter is passed by indirect laryngoscopy. Usually the procedure, even in bilateral cases, may be completed in 20 minutes.

During the last three years 180 lavages on fifteen patients have been recorded. The ages varied from 14 to 72 years.

No serious ill effects have been observed, though as much as 250 c.c. of salt solution have been often used in a single lavage. Five patients had one or more chills following treatments. The fever always subsided the following day. In three, arsenic had been given

intramuscularly following the lavage. In one, no arsenic had been given. In the fifth the chill occurred both with and without administration of arsenic. Apparently, then, the chill results from a stirring up of the infection, or toxic products, or both.

For the first five or six weeks the lavages were given once a week. After that, at intervals of two or three weeks. Usually the patient realizes when drainage by postural emptying is insufficient and comes in voluntarily.

What have been the results? Results were not good in five patients. In one the condition was so far advanced that no results at all were obtained by two lavages and treatment was discontinued. In this patient there was also a definite history of a treated acquired syphilitic infection. However, the history of her bronchiectasis dated back a good many years, probably antedating the syphilis. In another patient, no diagnostic lung mapping had been done. He had apparently an acute suppurative pneumonitis and it is now questionable whether lavage should have been done. A diagnostic bronchoscopy was done. He objected to further bronchoscopy and lavage was tried as an alternative. Three other patients showed no appreciable improvement.

In the other 10 patients, all had proven bronchiectasis either unilateral or bilateral. They were all improved. Subjectively, they felt better, raised less sputum, coughed less, and no longer noticed an odor.

Objectively there was: 1. Disappearance or marked diminution of odor when present. This may have been due in part to the concomitant administration of arsenic. 2. Gain in weight. One patient gained 15 pounds; another 17 pounds; and another 10 pounds. 3. A diminution in the amount of sputum. This is quite striking in some of the advanced cases. 4. Greater energy. 5. Cheerfulness replacing despondency. 6. More ready acquiescence to lavage than bronchoscopy.

However, the longer these patients are watched, the more certain facts become obvious. The advanced bilateral bronchiectatic is prone to acute pneumonic flare-ups, particularly with an acute respiratory infection. Eventually, with such an attack the right heart fails and the patient dies. Two of my patients who improved under treatment have since come to such an end.

In summary, it may be said that the bronchiectatic patient may be made more comfortable; happier; stabilized so to speak, but never cured by any means other than radical surgery. Even to accomplish conservative improvement requires every therapeutic

weapon at our command, viz., arsenic administration and sinus surgery when indicated and better drainage by posture, bronchoscopy or lavage. I feel the only advantages of the latter over bronchoscopy are: 1. Simpler and less expensive armamentarium is required. 2. Treatment can be made an office procedure. 3. It is less objec-



Fig. 1. Probable right lobar atelectasis in white female, aged 45 years, following a pneumonia four weeks previously. The flat plate suggests a basal atelectasis. However, bronchoscopy showed the right middle lobe only to be involved.

(Case 1)

tionable to some patients. 4. There is perhaps some advantage of the hypertonic salt solution over simple bronchoscopic aspiration with the use of a bland medicated oil, but this is debatable.

Finally, routine diagnostic bronchoscopy should always be done before any treatment is instituted.

ILLUSTRATIVE CASE REPORTS

The triangular, basal shadows of atelectatic, bronchiectatic lobes were first described by Singer and Graham.²⁰ The importance of prophylactic treatment of any type of atelectasis in childhood is obvious if the subsequent bronchiectasis is to be prevented. Such prophylactic care has been previously stressed and reported.^{10,18} A

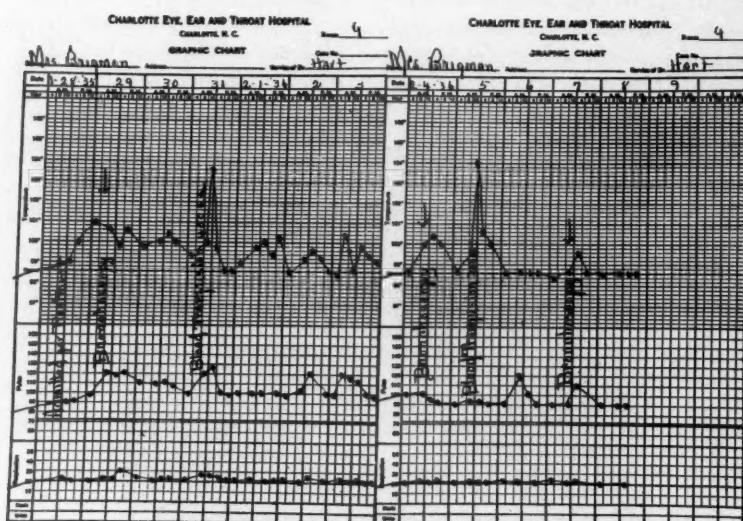


Fig. 2. Temperature chart showing the response to bronchoscopic aspiration and transfusions for her secondary anemia. This case is most important in the prevention of a subsequent bronchiectasis. (Case 1)

priori, the same care of atelectasis in the adult would seem to be important. It is germane to include such a case.

CASE 1.—Potential Bronchiectasis in Adult with Right Lobar Atelectasis. Treatment with Recovery.

The patient was a white woman, aged 45 years, first seen on Jan. 28, 1935. Productive cough with odor, and fever had persisted after pneumonia four weeks previously. Roentgenogram showed a homogeneous density occupying all the lower area of the right lung field and extending as high as the third rib anteriorly. Although there was no cardiac displacement this was interpreted as a lobar atelectasis. This was clinically confirmed by bronchoscopy because thick pus was aspirated from the right main stem bronchus and it was thought largely from the right lower lobe.

However, two subsequent bronoscopies showed the pus to be coming from the right middle lobe bronchus. This was a little surprising as the x-ray plate suggested a lower lobe lesion. The right lower lobe was probably involved secondarily due to the gravitation of pus. During this period she also had two blood transfusions for a rather marked anemia. She made a complete recovery.

This case was probably, then, one of the group of so-called unresolved pneumonias since there was no obstructing abnormal tissue or stricture. Such a condition might have been the prodrome to the bronchiectasis of the following case.

CASE 2.—*Unilateral Bronchiectasis Following Influenza. Treatment by Arsenic and Lavage.*

A man, aged 53 years, presented himself for examination on July 10, 1935. The complaint was cough. He stated that he had never had any trouble until after an attack of influenza two years previously. He denied pneumonia. A cough followed which did not become productive until two months prior to examination. He thought that he got up $\frac{1}{2}$ to 1 ounce of pus each 24 hours. There was nothing else pertinent in the present, past or family history.

The ear, nose and throat examination was entirely negative. Particular attention was paid to the sinuses.

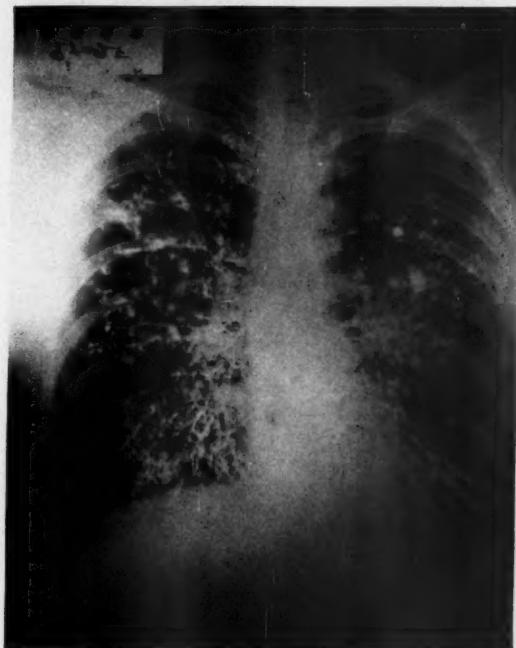


Fig. 3. Left sided basal bronchiectasis in a man, aged 53 years. The only antecedent factor was an influenza. He was improved by arsenic and lavage. (Case 2)

Bronchoscopic examination revealed nothing of importance except some pus with odor in both main bronchi (aspirated specimens were negative for fusiform bacilli, spirochetes and acid fast organisms). Twenty cubic centimeters of lipiodol was instilled into each side through the bronchoscope and a roentgenogram taken. This showed a moderate left sided bronchiectasis, but normal filling on the right. The pus on the right side, then, seen at bronchoscopy was just a spilling over from the involved side.

He was then put on bronchial lavage once weekly. Only the left side was lavaged using about 125 c.c. salt solution. This was done once weekly for ten weeks; and then every two or three weeks until 16 lavages had been given.

The first two were combined with 0.3 Gm. sulpharsphenamine intramuscularly because of the odor to the sputum.

The patient had been forced to stop work. He has now returned to full time duty and feels quite well. The odor disappeared from the sputum, the amount diminished, and he remained quite comfortable on postural drainage done once daily. He has not been seen in some time, however.

CASE 3.—Unilateral Bronchiectasis Complicating Neglected Foreign Body. Ultimate Lobectomy.

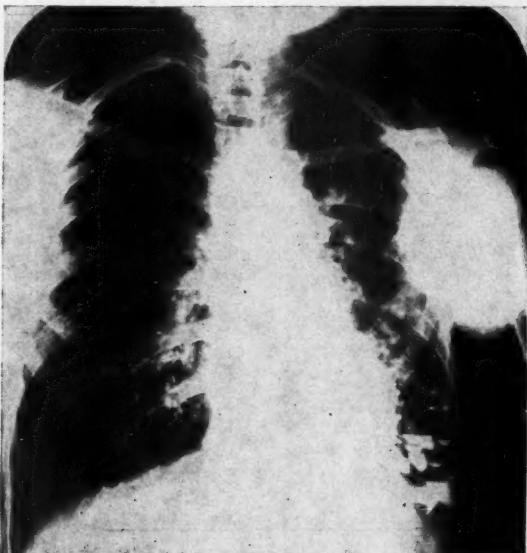


Fig. 4. Lung mapping of a 14 year old boy who 12 years previously had aspirated a peanut. The right side fills normally but multiple bronchiectatic cavities are present on the left with definite fluid levels. Repeated bronchoscopy made him a better surgical risk. Only lobectomy can cure such a case. (Case 3)

A white boy, aged 14 years, was referred to me on Sept. 3, 1931. There was a definite history of aspiration of a peanut 12 years ago followed by pneumonia and empyema. Surgical drainage had been done for the latter. His complaint was a constant cough productive of foul sputum.

The roentgenogram was reported as follows: "The left chest is markedly compressed (previous rib resection for empyema). There is a marked increase in density throughout the left lung which is more marked in lower half. There is no definite circumscribed abscess. There is some thickening on the right around the hilum, but the rest of the right lung field is normal. The heart is markedly pulled to the left, probably due to adhesions. The diaphragm is apparently normal."

There were, as one would expect, bizarre physical signs over all the left chest. There was marked clubbing of the fingers.

Bronchoscopy was done under local anesthesia, using a No. 6 bronchoscope. Some 250 c.c. of foul pus was aspirated from the left main stem bronchus. There was no stricture and no demonstrable foreign body (at this stage it had probably undergone liquefaction). Subsequent bronoscopies showed this pus to be largely from the lower lobe.

Lung mapping was next carried out, using 15 c.c. of lipiodol in each side of the bronchial tree. The subsequent x-rays showed normal filling on the right, but a marked basal multiple bronchiectasis on the left.



Fig. 5. A chest film of the same patient after a single stage lobectomy by Dr. E. A. Graham of St. Louis. His residual postoperative sputum was 15 c.c. due to a slight residual bronchiectasis of the left upper lobe. He was rendered fever-free and restored to normal life. (Case 3)

The laboratory report by Dr. L. C. Todd stated no spirochetes were found on dark field examination; a mixed infection with streptococcus predominating was also reported; and no tubercle bacilli. Other laboratory work was negative.

The patient was running an afternoon temperature of 99° to 101° F. He was instructed as to bed rest, high caloric feedings and postural drainage. A left phrenic exeresis was done by our surgical consultant on Oct. 2, 1931 with indifferent results. Due to adhesions a full rise of the diaphragm was not secured. Adhesions also prevented the use of pneumothorax.

During the next eighteen months I did a number of bronoscopies. This combined with his regimen at home reduced his temperature and made him a

much more favorable surgical risk. A large amount of pus was always present however.

At this stage I thought that the only hope for a long or useful life was radical chest surgery of the most skilled sort. He was, therefore, referred to Dr. E. A. Graham of St. Louis. Dr. Graham has since done a left lower lobectomy. He reported some residual bronchiectasis of the left upper lobe. Nevertheless, when last seen a temperature chart kept at home showed him free of fever. The cough and sputum were reduced to a point of little inconvenience (15 c.c.) and the chest wound was entirely healed. The following year he served as manager of his local high school football team.



Fig. 6. Right sided bronchiectasis in a man, aged 45 years, secondary to bronchogenic carcinoma proven by bronchoscopic biopsy. This again emphasizes bronchial obstruction as a predisposing factor particularly in unilateral bronchiectasis.

CASE 4.—Advanced Bilateral Bronchiectasis Complicated by Suppurative Sinus Disease. Treatment by Arsenic, Sinus Surgery, Lavage, and Deep Roentgen Therapy. Ultimate Death.

This young woman, aged 24 years, was first seen on July 10, 1935. Her complaint was productive cough. She had had a lung mapping done six years previously in Detroit with a diagnosis of bronchiectasis. Roentgen studies of her sinuses showed all involved with possible exception of the frontals, and the mucous membrane of these was thickened. She had previously had an intra-nasal antrum on the left, with removal of the left middle turbinate. Foul smelling pus was washed from each antrum. The blood Wassermann was negative. She had already had a course of arsenic by her family physician prior to admission.

Diagnostic bronchoscopy was done. A quantity of ill smelling pus was aspirated from each side. On the right it was apparently coming from both the middle and lower lobe orifices; on the left, largely from the lower lobe orifice. There was no evidence of obstructing granulation tissue, neoplasm, or stricture. The bronchoscopic specimens showed fusiform bacilli.



Fig. 7. Extensive bilateral bronchiectasis in 24 year old woman. She went through the gamut of sinus surgery, arsenic, bronchial lavage, and x-ray therapy. Although showing rather marked temporary improvement, she ultimately died of an acute pneumonic flare-up. (Case 4)

Lung mapping by the catheter method showed numerous large, bilateral bronchiectatic cavities. The process was extensive and advanced on both sides.

Subsequently two therapeutic bronchoscopies were done. She was then thought well enough to go ahead with necessary sinus surgery.

On July 29, bilateral radical antrum, ethmoid and sphenoid operation was done under local anesthesia. She made an uneventful convalescence, and the sinuses subsequently remained free of suppuration.

She was then started on bronchial lavage. At each treatment some 250 c.c. of salt solution was used: half on each side. At the same time further arsenic was given in five doses (0.3 Gm. sulpharsphenamine each) intramuscularly.

After 15 lavages, a second lung mapping was done. There were still bilateral, multiple bronchiectatic cavities. The change for the better, if any, was slight.

In all 40 lavages were done. She stated the sputum, which was excessive in amount, diminished one third. The odor largely disappeared. She gained 15 pounds in weight. Her health was better than in years. Despondent before treatment, she was cheerful and interested in life.



Fig. 8. Sinus roentgenogram of same patient showing extensive changes in maxillary sinuses and ethmoid labyrinth. Much pus was returned on irrigation of the sinuses. (Case 4)

In July, 1936, she had an acute flare-up requiring bronchoscopy. Lavage was later resumed.

In the spring of 1937 she was given a series of deep x-ray treatments. From these she received no benefit. Quite the reverse, as she came into the hospital in June, 1937, with a very acute pneumonic process. Despite three emergency bronchoscopies, she died on June 28, 1937.

CASE 5.—Advanced Bilateral Bronchiectasis Complicated by Suppurative Sinus Disease and Repeated Hemorrhage. Treatment by Arsenic, Sinus Surgery, Lavage, and Phrenicectomy. Ultimate Death.

A young man, aged 31 years, was first seen May 17, 1935. His complaint was repeated pulmonary bleeding. This had begun without any known reason two years previously and had continued at intervals to date. He had had a productive cough for a long time. There was nothing else of importance in the present or past medical history.

It is interesting to note that in his first examination there was nothing suggesting disease of the nasal sinuses. Bronchoscopy showed pus from both right middle and lower lobes and left lower lobe. Rather free bleeding was pre-

cipitated on the left and controlled only by the liberal use of epinephrine. There was no evidence of bronchial obstruction. The aspirated specimens showed no fusiform bacilli, spirochetes, or acid fast organisms. Lung mapping done at bronchoscopy showed a moderate multiple bronchiectasis involving the lower left, and right middle and lower lobes.



Fig. 9. Advanced bilateral bronchiectasis in a man, aged 31 years. His chief complaint was hemorrhage. Bronchoscopy showed this to be from the left side and it was controlled by phrenicectomy. He was considerably improved by sinus surgery, arsenic and lavage. However, death from an acute pneumonic flare-up eventually occurred. Here again, the hopelessness of these cases without surgery is emphasized as is the prophylactic bronchoscopic care of early chest lesions.

(Case 5)

A week later he began to bleed and this continued for twelve hours. Bronchoscopy was repeated and the blood shown to be coming from the left side. Phrenicectomy was advised on the left and done by a surgical consultant. This effectively controlled the hemorrhage and he had none subsequently.

Because of other experiences, his sinuses were x-rayed some two months later. There was a surprising change. The mucous membrane of both frontals was considerably thickened; both ethmoid labyrinths showed marked hyperplastic changes; both antrums exhibited marked opacities; the sphenoids were negative. Subsequent irrigation of the antrums through the inferior meati returned only a small amount of mucoid material from the left, but considerable thin pus from the right.

For these reasons a bilateral radical antrum and ethmoid was advised and done under local anesthesia on August 9. The sphenoids were also opened at the same time.

A week after operation bronchial lavage was begun. Because of some odor to the sputum, three intramuscular injections of 0.3 Gm. sulpharsphenamine were also given. Lavage was continued at weekly intervals for nearly four months. Lung mapping was then repeated by catheter technic. From such, it could not be said that the bronchiectatic cavities were any smaller.



Fig. 10. Sinus plate of same patient showing particularly the opacities of the maxillary sinuses. Irrigation proved suppuration in connection with the hyperplastic changes. The mucous membranes of the frontals and ethmoid labyrinth are also thickened (Case 5). Whether such infections are primary or secondary is still a debated question. There is no fixed rule. They probably are a primary and predisposing factor in some patients; in others wholly secondary. Nevertheless, the surgical eradication of such infections must be considered as part of the program.

Lavage was then continued every two or three weeks. In all he had 28.

As a result of the above treatment his general health was much improved. He stated his paroxysms of coughing had been less frequent and that his sputum had been reduced by one half. He gained ten pounds in weight.

However, in May, 1936, he developed an acute pulmonary flare-up. He did not come into the hospital until June 25. At that time, he had a failing right heart and died in less than 24 hours despite emergency treatment by our consulting internist.

SUMMARY

No proven cases of so-called congenital dry bronchiectasis have been encountered. These are probably rare.

Any unresolved pulmonary suppuration in childhood is apt to be a precursor of a later bronchiectasis. This is also true of adults. Particularly is this true if basal atelectatic areas are present as so ably demonstrated by Singer and Graham²⁰ and later by Anspach¹⁰. Bronchoscopic aspiration is an ideal method of prophylactic treatment in these cases.

Unquestionably, neglected foreign bodies are a frequent cause of unilateral bronchiectasis. The recent work of Weinberg⁴ confirms previous reports and re-emphasizes bronchial obstruction of any sort as a cogent factor in the production of unilateral bronchiectasis.

It is felt that suppurative sinus disease may be an etiologic factor in bronchiectasis. The distinction has been made between true suppuration and merely hyperplastic changes. The latter offer a more questionable relationship.

Infection may also occur secondarily. It is pertinent and interesting to note here that none of the cases to which reference has been made had a clinical or family history of allergy.

Only 3 of 13 cases of proven bilateral bronchiectasis had merely hyperplastic changes in one or more sinuses. In a fourth there was no x-ray record but no clinical evidence of sinus infection. All the others had true suppurations. Conversely, only one of six cases of proven unilateral bronchiectasis had a suppuration of the sinuses. This would seem to point to them as causative factors in some of the bilateral cases.

Disregarding the etiologic element, sinus suppurations are thought to be important therapeutically. Improvement with any therapy would be difficult with constant re-infection by a post-nasal purulent discharge. I have undertaken radical sinus surgery under local anesthesia before instituting treatment. Diagnostic bronchoscopy should precede any treatment in all cases.

Bronchial lavage by the Stitt method was then undertaken. Arsenic was used as an adjunct when indicated.

By following this plan, both subjective and objective improvement was noted in all cases treated except five. However, these patients are never cured by such treatment. They are stabilized, and they are made happier and more comfortable. Even though show-

ing considerable temporary improvement, death waits around the corner for the patients with advanced bilateral bronchiectasis.

It is felt that the Stitt method of lavage has a useful but limited place in therapy. No serious results have been encountered in 180 done in the past three years. However, like any other treatment, it must be used as only part of a systematic program. To get improvement in advanced cases, every weapon at our command must be utilized. Only modern thoracic surgery can bring about a cure. Recent surgical progress now offers hope to even the bilateral cases.

Illustrative cases are appended to demonstrate the points in question.

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DIAGNOSIS AND TREATMENT OF LATERAL SINUS THROMBOSIS

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SEPtic thrombophlebitis of the lateral or sigmoid sinus with the concurrent blood stream infection is still the major problem of the otologist because it is the most common serious complication of mastoiditis. Fortunately, this occurs in only about 3 per cent of the reported cases of mastoiditis, and the mortality has been reduced from 50 per cent to 25 per cent in the past twenty-five years.

A thrombus in the lateral sinus was first recognized by Hooper¹ in 1826 and the internal jugular vein was first ligated by Zaafal² in 1880, but the first successful operation for thrombosis of the lateral sinus was done by Arbuthnot Lane³ on Aug. 18, 1888:

The patient was a child with right chronic purulent otitis media, mastoiditis and classical symptoms of septicemia with swollen optic disc, the right more than the left. At the second mastoid operation a necrotic sinus was uncovered containing pus which was removed until quite healthy clot was obtained. The internal jugular vein was ligated. This patient recovered. In a second patient operated upon four months later, no thrombus was found in the sigmoid sinus and the internal jugular vein was not ligated. This patient died with bronchopneumonia. Thus at the beginning, lateral sinus thrombosis was treated by two surgical methods—ligation and non-ligation.

The clinical picture, drawn by Lane fifty years ago, has changed very little today in spite of the fact that our methods of diagnosis, treatment and surgical technic have been improved greatly.

Otitis media, mastoiditis, fever, nausea, vomiting, headaches, chills and mental or emotional disturbances form the basis for investigation by laboratory and other methods leading to the diagnosis of lateral sinus thrombosis. When a patient has a middle ear or mastoid infection and there occurs a sudden rise of temperature to 104 degrees or more, usually preceded by a chill or a chilly sensation, with recession to normal or subnormal in a few hours, always think first of sinus thrombosis. This septic rise may occur a few days, weeks or months after the otogenic infection has begun. It is of a septic type with wide excursions. There may be periodic elevations which in the presence of other signs are significant. The patient often is comfortable between the high elevations. This septic type of temperature often occurs in hemorrhagic mastoiditis but

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usually with the aid of a blood transfusion subsides in two or three days after mastoidectomy has been done. This is probably due to a phlebitis of the smaller venules.

The temperature occasionally occurs in the pneumonic and typhoidal types. Afebrile types are rare—there are usually no other symptoms and the thrombus is accidentally discovered.

Chills precede the rise of temperature in the majority of cases but they may not be present or not recognized, especially in young children. Headaches, nausea, vomiting and signs of meningeal irritation occur more frequently in children. The ocular symptoms, tortuosity of the retinal veins and papilledema of varying degrees, appear in about half of these cases, mostly when there is an obliterative thrombus.

The presence of adenitis or tenderness on palpation along the course of the internal jugular vein from the bulb downward, is of confirmatory value, especially in cases of bilateral mastoiditis.

The Toby-Ayer⁵ otologic application of the Queckenstedt test demonstrates the presence of an obliterative thrombus in the lateral sinus. This is a valuable diagnostic test when positive. It can indicate the side involved in bilateral mastoiditis. Griesenger has described edema over the mastoid extending to the eye due to thrombosis of the emissary vein and engorgement of veins. This sign, when present, may be of some value.

Metastasis is conclusive evidence of a bacteremia. It is characterized by development of pain in the joints with abscess formation, superficial abscesses or involvement of more vital structures during the course of mastoiditis either before or after operation. Anomalies of the anatomic structure of the cranial sinuses may alter clinical signs and tests. Ersner and Meyers⁶ first stressed the importance of x-ray study of the variations of the lateral sinus in relation to thrombosis. More recently Woodhall and Seeds⁷ have correlated radiographically the anatomic, clinical and pathologic findings in these cases. Cody⁴, reviewing the literature in which the location of the thrombus was specified, noted that in 426 cases, approximately 31 per cent occurred in the lateral sinus and jugular bulb, 31 per cent in the sigmoid sinus, 13 per cent in the jugular bulb and 25 per cent without thrombus.

The differential diagnosis by Kopetsky⁸ between hemorrhagic mastoiditis and coalescent mastoiditis has been a great aid to the otologist in diagnosing sinus thrombosis. Sepsis often appears from the onset in the hemorrhagic type. If it appear suddenly in the course of an ordinary convalescence in this type, sinus phlebitis may

be suspected. In coalescent mastoiditis signs of blood stream infection usually appear suddenly later in the course, or they may develop more gradually from the onset as a result of a thrombosis. A blood culture should be taken on the high rise of temperature when sepsis is suspected. A positive culture when there is no chance of contamination is conclusive evidence of sinus phlebitis but a negative culture means little. Sometimes the organism is not visible on the culture medium for three or four days. Blood cultures should be made each day.

An occluding thrombus may be sterile and cause no bacteremia.

A series of complete blood counts is important in diagnosis. A decreasing red cell count and hemoglobin with increasing white cells ranging from 15,000 to 22,000 and a Schilling hemogram shifting to the right usually indicates the presence of a hemolytic streptococcus, the most frequent organism in sinus phlebitis.

Direct examination of the lateral sinus after it is completely exposed is necessary before making a definite diagnosis. The vein should be palpated to determine the thickness of the wall, and its color noted. The upper and lower ends should be compressed carefully and the flow of blood noted. If the infection has spread by direct continuity there may be granulations on the venous walls or an abscess draining through the sinus covering. In bilateral mastoiditis, if the sinus first suspected appears normal, the other side should be examined. If both sinuses appear normal and there is a blood stream infection one must consider all available information, such as the length of time of each mastoiditis, the severity of each, all positive signs, and use good and careful judgment before obliterating one of the sinuses. However, Kopetsky told me that he had obliterated both sinuses at the same operation and the patient recovered.

Treatment for otogenic sepsis and sinus thrombosis might be classified as prophylactic, supportive and surgical. The prophylactic treatment should be given in every middle ear and mastoid infection as soon as a culture is made from the discharging ear and the predominant organism determined.

Leading serologists have demonstrated the great value of pneumococcus vaccine in preventing intracranial complications in the lower animals. Kolmer and Anano in 1932 demonstrated that immunization with types I, II and III pneumococcus autogenous vaccines afford protection against experimental meningitis in rabbits. They were successful in protecting 57 per cent of their rabbits by intracutaneous injections.

Goldman and Herschberger¹⁰ reported that in 56 cases of acute mastoiditis due to infection with pneumococcus type III, the vaccine was administered and only four patients died. Of these, two deaths were not attributed to the mastoid infection.

Kolmer⁹ states that prophylaxis may be aided by intramuscular injections of polyvalent anti-streptococcus serum. From the stand-point of treatment of septicemia due to hemolytic streptococci he is in favor of early administration of this serum in large doses intravenously, every 8 to 12 hours for at least 4 to 6 doses. In staphylococcal septicemia there is not so efficient a serum.

Murry and Best¹¹ have done some recent research with heparin in the prevention of thrombosis. This may prove of value in cases of sinus thrombosis.

The supportive treatment consists in maintaining the proper nutrition, frequent small blood transfusions and immunization. Transfusion with whole blood, preferably from a donor convalescent from the same organism, should be given in small quantities every three or four days, dependent on the condition of the patient. This has an antibacterial action and supplies the patient with fresh leukocytes, complement, agglutinins and opsonin. It has so far been our best therapeutic agent in combating streptococcus hemolyticus infection in the blood stream and fixed tissues. Transfusion with immune human serum is good. The intravenous use of dyes has been practically discarded. Pregl's iodine and metaphen still are recommended by Kolmer⁹ for staphylococcal septicemia.

Para-amino-benzene sulfonamide (sulfanilamide) and its derivatives are potent chemotherapeutic agents in the treatment of hemolytic streptococcus infections and have some value in pneumococcal and meningococcal infections. It is still in the experimental stage.

In sinus thrombosis and septicemia surgical removal and drainage of the primary and secondary foci of infection is the most important factor in treatment. Surgery of the mastoid or the sinus should be done only when a leukocytic wall has been established. It should be performed gently and quickly in order to minimize any shock or hemorrhage. All infected bone and clots should be thoroughly removed and free and continuous drainage secured.

A complete simple mastoidectomy must be performed first always, then the lateral sinus is uncovered and carefully inspected. When the diagnosis of thrombosis is determined the internal jugular vein should be ligated in the majority of cases. This is the same procedure that was employed fifty years ago and is still the safest and

best today. There has been great controversy among otologists for a number of years as to whether it is better to resect the internal jugular entirely in all cases or to ligate above or below the facial branch. Some prominent otologists oppose both operations, depending on blocking and draining the sinus to eradicate the septic clot and infection. Cases of sinus thrombosis without apparent symptoms have been discovered by chance during mastoid operations or postmortem, indicating that nature is able to take care of the infection only by blockage above the jugular vein. Septicemia and metastases may occur after ligation of the jugular vein, showing that this operation cannot be depended on entirely to prevent bacteria from entering the blood stream. It has been demonstrated that it is possible to inject all the cranial sinuses via the external jugular vein with the internal jugular ligated.

It is erroneous to say that any one surgical procedure should be adopted in all cases. Coalescent and hemorrhagic mastoiditis behave differently clinically. The symptoms are more marked early in the disease with the latter type. There may be a small thrombus in the emissary vein or small mural clot on the intima of the sinus wall. In such cases the infection can be controlled without surgery of the jugular vein. If the infected thrombus is extending into the jugular bulb or there is suppuration below the bulb, it would be wisest to resect the internal jugular vein. It is best to adopt the method and extent of the operation to suit the findings in each case.

Surgery on the jugular vein is best done by two teams of surgeons, as it will save time and lessen the liability of infection in the neck. When this is done the lateral sinus should be blocked at the torcular and jugular bulb ends, and incised. Any clot in the infected sinus or bulb should be removed. The packing should be removed from above, then below to determine if free bleeding exists, and if so, it should be repacked. Several small plugs of gauze should be packed tightly in the sinus. If free bleeding is not obtained it is necessary to extend the operation until the venous wall of the sinus looks normal, free bleeding is found and sufficient drainage is secured.

THE IMPORTANCE OF PHYSICAL EXAMINATION IN THE DIFFERENTIAL DIAGNOSIS OF CHRONIC PULMONARY DISEASES

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ROENTGENOSCOPIC and bronchoscopic examinations have assumed such a prominent place in the recognition and differential diagnosis of chronic diseases of the chest that physical examination of the thorax is gradually becoming a lost art. My purpose is not to minimize the value of roentgenoscopy and bronchoscopy in the diagnosis of thoracic diseases, for in many cases the information obtained by these examinations cannot be secured in any other way. However, it seems proper to direct attention again to the fact that signs valuable in the recognition of pulmonary disease can be obtained by inspection, palpation, percussion and auscultation, and that the employment of every method of examination is required if errors in diagnosis are to be reduced or avoided.

Physical examination is particularly valuable in the differentiation of the various types of lesions which involve the hilar areas and produce identical roentgenoscopic findings. Tuberculosis usually produces significant physical signs if the disease is located in the periphery of the lung, but when the lesion involves the hilar or basal areas, physical signs may be absent. The absence of signs may be of value in differentiating infiltration due to tuberculosis from that due to carcinoma.

Unless the lesion in the bronchus produces complete obstruction in tuberculosis, breath sounds may be quite normal, whereas in carcinoma, with the same degree of bronchial occlusion, breath sounds are greatly diminished or absent. Absent or diminished breath sounds over any area of the lung with little or no impairment of the percussion note should always suggest the presence of carcinomatous infiltration, and when these signs are present tissue should be removed from the wall of the bronchus supplying this area of the lung, even though bronchoscopic inspection has failed to reveal significant infiltration in the bronchial wall. When a small carcinomatous lesion is located on the left side behind the heart, the lesion may not be demonstrable by roentgenoscopic examination; yet physical examination almost always reveals the presence of the disease. Physical examination of the thorax is never complete without careful palpation of the supraclavicular areas in search of a metastatic lymphatic node, commonly known as Virchow's gland.

In cases of pulmonary abscess physical signs are usually absent, although tenderness may be elicited by pressure on the wall of the thorax over the site of the infected area in the lung. The sputum from abscess is almost always malodorous, and the appearance and odor of the sputum may be of considerable value in the differentiation of tuberculous and nontuberculous pulmonary disease.

Extensive chronic bronchiectasis may reveal little or nothing on physical examination, but the production of a large amount of foul, purulent sputum, when the patient assumes a kneeling posture with inversion of the thorax, is indicative of a bronchiectatic pulmonary lesion.

The physical signs of a foreign body depend entirely on the size, shape and location of the substance that has been aspirated and the length of time that it has been present in the bronchus. Atelectasis or emphysema are both characteristic of a foreign body, depending on the degree of bronchial occlusion. Distant breathing is usually present over the area of distribution of the occluded bronchus. In other cases the physical signs of a foreign body consist of a few sonorous rales at the base of a lung. Regardless of other findings, the sign of a localized unilateral pulmonary lesion indicates the advisability of bronchoscopic examination.

Unless pneumoconiosis is complicated by tuberculous disease the physical signs may be limited to those ordinarily encountered in chronic emphysema. Even when tuberculosis is a complicating factor, dilatation of the alveoli may mask the signs that are ordinarily produced by tuberculous infiltration. Rhonchi, which so frequently are heard in cases of asthma and chronic asthmatic bronchitis, usually make it difficult or impossible to detect other lesions in the lung on physical examination.

One of the most significant physical signs is stridor which, without changes in the voice, usually indicates an obstructive lesion in the trachea or a large bronchus, although it may be elicited when a stricture is present in a secondary bronchial division. Stridor may also be present in patients having extensive pulmonary fibrosis, and bronchoscopic study is frequently required to differentiate fibrotic change from that produced by partial tracheal or bronchial occlusion.

Differentiating the density observed in consolidation or atelectasis of the lung from that produced by effusion may be difficult on roentgenoscopic study. In such cases physical examination is indispensable, although at times the presence or absence of fluid cannot be determined without thoracentesis.

Roentgenoscopic examination of the thorax in cases of diaphragmatic hernia may indicate the presence of primary pulmonary disease when careful physical examination will at least suggest that the findings are not the result of disease of the lungs or pleura.

CONCLUSION

The recognition and differential diagnosis of chronic pulmonary diseases require the utilization of all methods of examination. Improvement in our methods of securing direct and indirect visualization of the lungs and bronchi should not decrease our efforts to obtain the information that may be gained by careful physical examination of the thorax.

THE DEVELOPMENT OF THE VARIOUS METHODS OF URETERAL TRANSPLANTATION AND CYSTECTOMY

The Addition of Another Method

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Charlotte

VARIATIONS in surgical technic develop so rapidly that not only the procedures of a few years past but even the original method and principle of the operation may become obscured.

The basic principle of all ureteral transplantsations was laid down by Coffey¹, when in 1909 before the Southern Surgical Association he reported his results in experimental implantation of the common bile duct in an oblique submucosal position, and suggested that the same principle might be applied to the ureters. This principle was successfully executed by C. H. Mayo in February 1912, with a ureter in a case of exstrophy of the bladder.

This principle of passage of a compressible tube through the wall of a hollow viscus, in imitation of the run of the common bile duct through and between the muscular and mucous coats of the gut must be carried out precisely to obtain efficient valve action. The success of the valve thus formed is dependent upon the maintenance of an intravisceral pressure and, preferably, an alternating pressure from within, as exists in the duodenum and bladder. In the duodenum such a pressure is assured. In the bladder and in the rectosigmoid congenital or acquired defects may affect the competency of the sphincters, so the competency must be proved by the ability to hold air and fluid.

There are several other factors affecting the efficiency of the valve: a. The ureter itself must be picked up from behind the peritoneum carefully, not stripped so closely as to interfere with its blood supply. b. Its straight course must be maintained without tension or torsion. c. The approximation of the ureter to the gut should be at a location where the gut naturally falls against the ureter so that it will remain there without tug upon the segment implanted. d. The bowel should be sutured over the implant behind the peritoneum and the entrance and exit of the ureter be covered by peritoneum, allowing the ureter to pass down behind the peritoneum, dip into the gut, and continue straight to the bladder.

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A low position therefore, below the brim of the pelvis, should be chosen on the right side and a higher position at and above the brim of the pelvis on the left side. e. The implants should not be made at the same level, nor should the ureters be made to converge in a T incision in the gut, because it is difficult to bring both ureters comfortably to the same site in the gut, and because too bulky infolding encroaches upon the caliber of the gut. f. A wide dissection of the muscularis from the mucosa should be made, so as to give the implanted segment of the ureter loose surroundings, when the muscularis and serosa are united over it. In fact, the ureter should be laid loosely in its new channel so that it can be moved up and down. The ability to slide the ureter between the layers of the gut allows an easier adaptation of the gut to the ureter, when the peritoneum is finally stitched around the anastomosis.

Failure to observe the above points probably explains the failure of as many ureteral transplantations as the improper and careless placement of the ureteral end in the intestine.

In fact, Walters² and Cabot at the Mayo Clinic, and Ladd and Lanman³ at the Children's Hospital in Boston, observing carefully these points in carrying out a technic very similar to the original Coffey-Mayo procedure, have attained excellent results. Walters operated in 26 cases with one death, Cabot 20 cases without a death, and Ladd and Lanman 15 cases with one case of peritonitis and fistula, with recovery. Ladd and Lanman isolate the stretch of gut used to receive the ureter with right angle clamps to hold back the contents and open the intestine with an electro-cautery. They pay special attention to the proximal end of the ureter, which they split longitudinally on the posterior wall. They then spread it with a stitch which they pass from the lumen of the intestine through the bowel to anchor it.

Walters mentions that the appearance of urine in the rectum in their cases varied from a few hours in some cases to several days in others. Ladd and Lanman report that the urine appeared in all their cases within 48 hours. The delayed flow of urine is probably due to edema and obstruction at the site of anastomosis. Beyond slight dilatation of the renal pelvis and calices and ureter, no permanent damage was seen at the Mayo Clinic. Helmholtz and Colts found that there was no apparent effect on the clinical results, as evidenced by renal function.

In every technic tried out in his experimental implantations, Kirwin⁴ observed late hydronephrosis and pyonephrosis. He attributed these to interference with peristalsis in the lower end of the

ureter on account of tension, altered blood supply, trauma or cicatrix. Yet in a study of 59 out of 76 cases at the Mayo Clinic, 50 per cent had no evidence of renal infection or stasis.

Again, it is at least suggested that the results must vary with the care in observing the points necessary for an efficient anastomosis. And when these technical steps in the operation are painstakingly carried out, as by Walters and Cabot, and Ladd and Lanman, the results carry a tremendous argument in favor of an operation closely approximating the original Coffey-Mayo technic.

Although Walters and Cabot and Ladd and Lanman have found no evidence of appreciable infection at the site of the uretero-intestinal anastomosis, theoretically at least, and actually in the hands of many surgeons, opening the intestine for direct implantation or implantation with catheters sometimes causes soiling that results in infection and drainage, if not in peritonitis and death. Ladd and Lanman reported one case of peritonitis in 15 cases operated on since 1930, and state, "The methods used for the treatment of exstrophy of the bladder at the Children's Hospital before 1930 were unsatisfactory. The operative mortality from peritonitis was high." Coffey himself sought through his second method to transplant both ureters at a time with catheters, evolving an elaborate technic of bowel cleansing and entering the bowel twice. Again there resulted peritonitis, sloughing of anastomosis and ureteral ends, difficulty in maintaining a free flow through the catheters. Comparison of results with double catheter implantation at one time should not be made, because there may be delay in the flow of urine due to paresis or edema in the ureter or intestine at the site of implantation after any method, with consequent obstruction to the flow of urine from both ureters.

Coffey, with his third method, severed and tied off one ureter at a time, placed it in the submucosal position, and anchored it to the full thickness of the bowel at its tied-off end. Then he pierced the ureter and the bowel mucosa with a transfixing and necrosing suture. Brenizer⁷ suggested and used a small metal ring either passed up the rectum and rolled into position or swallowed by the patient and picked up at the desired location. The ring assured the passage of the necrosing suture into the bowel, obviated Coffey's difficulty of too tight or too loose a necrosing suture, and held the suture in a fixed position, with the ureter on one side of the intestinal mucosa, the ring on the other. The necrosing suture was made to cut through by the contraction of the bowel on the ring and by tugging on a thread also tied to the ring and emerging from the anus. This

method obstructed the ureter for a few days, producing a temporary hydronephrosis.

Ferguson⁵, in his experiments on cats, placed a segment of the ureter in the submucosal position and closed the muscularis and serosa over it, leaving the ureter intact on both sides with the urine running through it to the bladder, and sought to sever the ureter through the rectum. Higgins⁶ elaborated this simultaneous implantation of both ureters and employed Coffey's necrosing suture. Brenizer⁸ employed the method of Ferguson and Higgins, using the ring and necrosing suture.

Walters objected to the necrosing suture, as elaborated by Higgins, saying that: "In an experimental study of the so-called aseptic, suture necrosis method, Mann and I found that immediate or eventual hydronephrosis occurred so frequently even though urine appeared in the rectum from the fourth to sixth day in most cases, that I have been fearful to use the method clinically."

Higgins⁹ in 1934 said: "I have collected a series of 52 cases with three fatalities. We are more than enthusiastic over the results we have secured with its use during the past year."

In 11 cases in which 20 ureteral transplants were done by Brenizer employing the ring and necrosing suture, all patients have done well with the exception of a girl, 18 years old, who had already developed considerable hydronephrosis; occasionally she still has attacks of slight pain and fever. Brenizer⁸ then placed both ureters in the submucosal position, straddled the lower portion of the ureters with a hairpin wire and passed the two ends of the wire down a catheter and out the anus. After 10 to 12 days, when both ureters were embedded in the intestine and urine was still flowing through them on both sides to the bladder, he applied an electro-cutting current to the wire's ends below, thus quickly cutting through the ureter and intestinal mucosa and completing the anastomosis.

Douglass and Edwards,¹⁰ in their experimental studies of the various methods of uretero-intestinal anastomosis, concluded in part from 67 experiments:

It is apparent that there are many advantages in allowing the ureters to become firmly healed within the wall of the bowel before a communication is established between them.

The first stage of Ferguson's operation immediately produces partial blocking of the ureter, due to swelling, induration, and hemorrhage in the bowel wall which surrounds the ureters and, in a lesser measure, to ureteral denervation. The obstruction is manifested by diminution in the output of urine and an increase in non-protein nitrogen of the blood which, in the average case,

reaches a maximum of 100 mg. on the fifth day. The obstruction has always been spontaneously relieved, usually by the fifteenth postoperative day, and has occasioned no demonstrative permanent renal changes.

Ferguson's (Higgins) first stage operation has an exceedingly low primary mortality and is followed by no permanent impairment of renal function.

When wires were looped over the ureters in dogs and allowed to remain in place 10 to 14 days, they often obstructed the ureters to such an extent that the animals did not long survive their removal.

In the human, where the cooperation of the patient permits the ends of the wire to clear the anus, the tendency to obstruct may possibly be largely removed. . . . The tendency of the wire to obstruct the ureters in dogs may be due to the fact that it was necessary to leave the ends of the wire fastened together by a shot well within the anus. This allowed the wires to ensnare the (hardened) contents of the bowel. In time, the weight of the impaction plus the efforts of the bowel to expel it by increased peristalsis produced such traction on the wire loop that the ureters could not function.

We have been unable to prevent obstruction in dogs by the use of indwelling ureteral catheters for two reasons: first, the dog's ureters are very small and will not admit catheters large enough to adequately maintain urinary drainage for a period of ten days or more; secondly, it is practically impossible to keep catheters in place long.

Quite recently Brenizer has described a two-stage method of transplanting the ureters in the bowel (Ferguson, Higgins, Brenizer, without catheters). His second stage was performed through the rectum with the aid of wires (straddling the ureters and passing down a catheter and out the anus) and an electric current, necessitating, therefore, only one abdominal operation. He performed this operation on a woman with irreparable vesicovaginal fistula. So far as we know, he is the first to utilize this plan of uretero-intestinal anastomosis in the human.

The severing of the ureters, following the Brenizer technic, is a second stage procedure, it is true, but it is not to be considered of great moment, and certainly not a second operation. It is done in a few seconds and annoys the patient no more than the removal of a drain. Of course, the removal of the bladder is a second stage operation.

Brenizer's technic is very simple and time sparing:

Both ureters are placed in the submucosal position and covered down to the lower angle of the incision through the serosa and muscularis. Then, the ends of a No. 1 tonsil or nasal wire bent in the form of a hairpin is passed down the ends of No. 18 to 20 whistle tip catheters and the covering by muscularis and serosa completed. Both layers of the incised peritoneum where the ureters are raised are stitched to the bowel placing the suture line covering the ureter extraperitoneally. The loop of wire around the ureter is pushed down into the rectal catheter until a patent loop remains open around the ureter. This loop around the ureter may be enlarged or diminished by holding the catheter and pushing upward or pulling downward on the wire or the whole wire-in-tube may be moved up and down to prevent pulling on it. The wire ends emerging from the catheter at the anus are bent back into a slit made in the

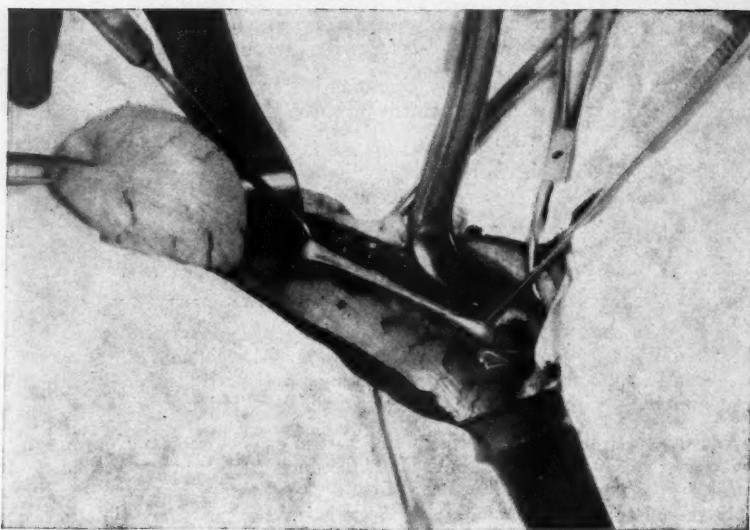


Fig. 1. The ureter and rectosigmoid are exposed. The ureter has been very carefully liberated retaining blood supply. The retroperitoneal bed is to receive the line of anastomosis when the ureter is transplanted.

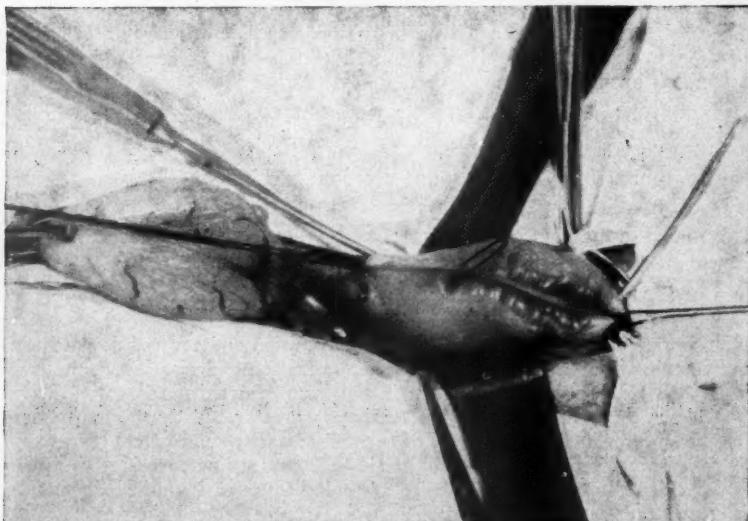


Fig. 2. The muscularis has been cut to the mucosa; the ureter is laid upon it; a No. 1 tonsil wire has been made to straddle the ureter so that both ends of it pass through the mucosa and down a No. 18-20 whistle-tip catheter. The muscularis and serosa are to be closed over the ureter and wire.

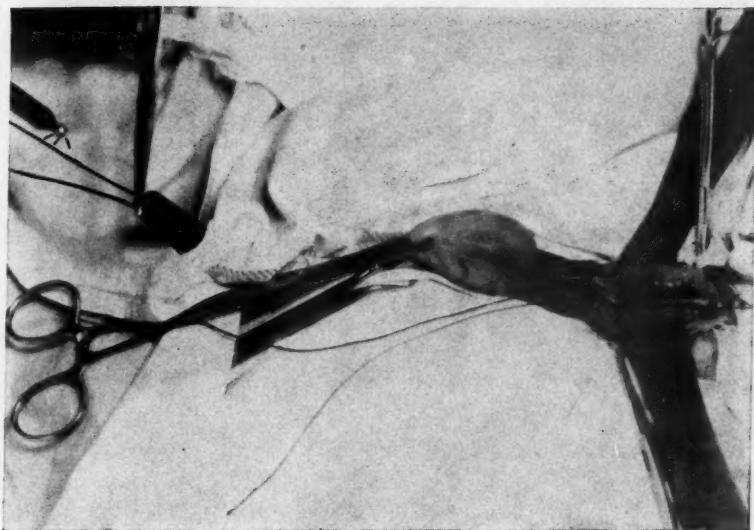


Fig. 3. The wire is seen pulled down on the ureter and emerging from the catheter at the anus. A strong, quick electro-cutting current is being applied eight to ten days after implantation of the ureter.



Fig. 4. The ureter in the submucosal position, No. 1 tonsil wire piercing fold of mucosa.

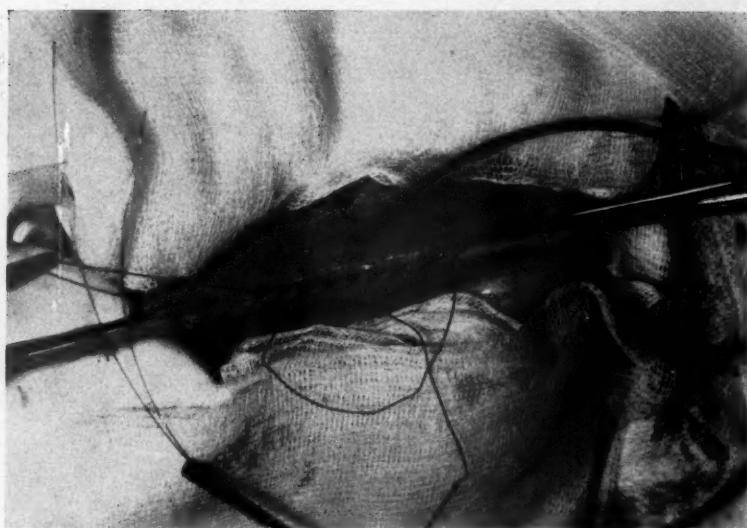


Fig. 5. Tonsil wire passing out through No. 8 ureteral rubber catheter and the catheter in turn between mucosa and muscularis. The stitch line in the gut and the passage of the catheter is placed extraperitoneally and the catheter made to pass out a stab wound in the side, guarded by a Penrose drain. On the eighth to tenth day the ureter is severed and thus made to communicate with the lumen of the sigmoid, simply by applying a high and quickly cutting electro-cutting current to the wire ends. First one ureter is cut, its flow proven by intravenous urography, and then the other ureter is cut and the urine flow similarly proven.

catheter. After the ureter has become embedded and healed in the intestine, preferably on the eighth to tenth postoperative day, each ureter is severed by pulling the wire loop further down into the catheter, and by pulling down on the catheter and applying an electro-cutting current to the emerging wires. There is practically no charring at the point cut, the proximal ends begin to discharge urine immediately, and the distal cut end of the ureter heals.

The great advantages of this method are:

1. The comparatively easy abdominal operation, with implantation of the intact ureters.
2. The subsidence of partial obstruction from edema, hemorrhage or denervation of the ureter before the ureter is cut.
3. The firm healing of the ureters within the intestinal wall, and no leak around the ureter before a communication is established between them.
4. The easy severing of the ureter into the bowel without second operation.
5. The comparatively easy anticipated cystectomy, done in a dry field and with disregard of the ureteral stumps.

Brenizer's method of severing the ureters at a distance, by means of a wire looping around the ureter and passing down a catheter emerging from the anus, by applying an electro-cutting current to

the exposed wires is a new and original conception, first carried out on dogs and then employed in the human.

Douglass and Edwards in their experiments on animals did not make use of the wire in the way Brenizer has described and rightfully interpreted their results due to obstruction caused by the wire, held together with a shot, becoming ensnared by the hardened feces in the dog. Their troubles have arisen: 1. By using a silver wire too malleable to be passed down a catheter and thus avoid entanglement in the hardened feces of the dog. 2. They used no way of keeping the loop around the ureter open, and allowed the taut wire to compress the ureter. 3. They had no way of releasing and tightening the loop around the ureter, by either moving the wire up and down in the catheter or by moving the whole catheter with wire arrangement up and down. 4. They had no way of jacketing and insulating the wire in the catheter, so that the electro-cutting would be confined to the loop around the ureter.

Indwelling catheters, or any foreign body in the ureters, in any ureteral transplantation are likely to do more harm than good and may be the cause of slough and infection. This point was largely proved by Lanman and Colby,¹¹ and most operators now avoid the use of catheters. I have not found them necessary either to identify the ureters or to keep the flow going in my operation. Just now I am working on a further modification of the technic in the attempt to use the Ferguson implantation of the intact ureters and then embed a No. 7 or 8 ureteral rubber catheter, containing a fine wire with the loop around the ureter. This small catheter I propose to allow to run parallel with the lower end of the ureter and emerge with it behind the peritoneum at the lower end of the incision into the gut, and out through a small incision in the flank, guarded by a Penrose drain down to the point of emergence? This same principle is used in a catheter ileostomy, and on withdrawal of the catheter the two serous surfaces come together to prevent leakage. Even though there were a slight leakage and soiling, the wound would be drained and would close in the same way the wound closes after ureterotomy for stone. There are several points to be investigated:

1. Will the catheter lying parallel to the lower stretch of ureter obstruct it?
2. Will there be leakage and soiling on the withdrawal of the ureteral catheter and wire?
3. If there be slight leakage and soiling, will it be of any moment in the presence of the Penrose drain and outside the peritoneum?

The execution of this last method is quite easy, and avoids all manipulations from below, and keeps the whole operation clear to view. The loop around the ureter and through the bowel mucosa is easily performed, merely by picking up a fold of mucosa, piercing it with a No. 1 nasal wire, leading the wire out the catheter. The catheter is covered along with the lower stretch of the ureter and led out in the extraperitoneal position through a small counter incision.

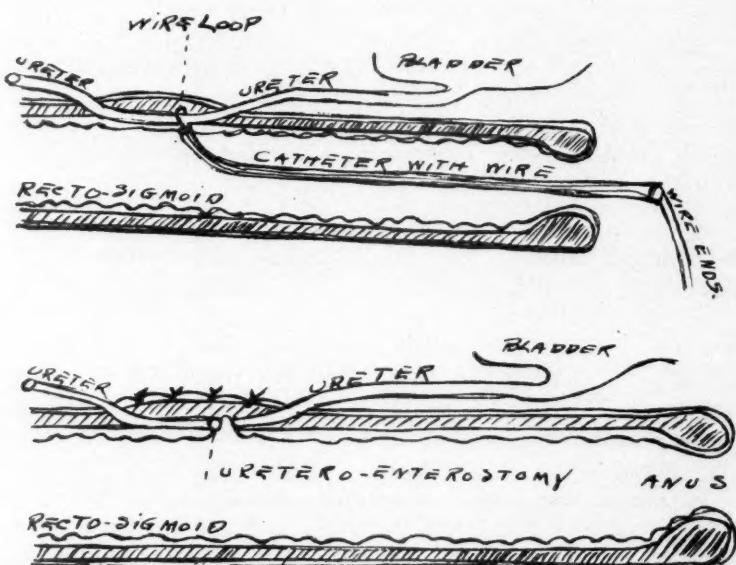


Fig. 6. Diagram illustrating position of wire loop over ureter, both ends, passing through mucosa and out whistle-tip catheter. The ureter is severed by applying electro-cutting current to wire ends.

My work so far convinces me that this method will be successful in the human, and will relieve such a patient as the one just operated on two days ago. This man had a carcinoma of the bladder involving the trigone of the bladder. There were dense adhesions in the pelvis. He had previously been operated on for typhoid perforation, for appendicitis, for ureteral stone, and had drained long through a fistula. The cancer had spread over the prostatic urethra; it was almost impossible to catheterize him, and his bladder was so contracted that he passed little urine. His only relief, while he did live, was a double ureteral transplantation.

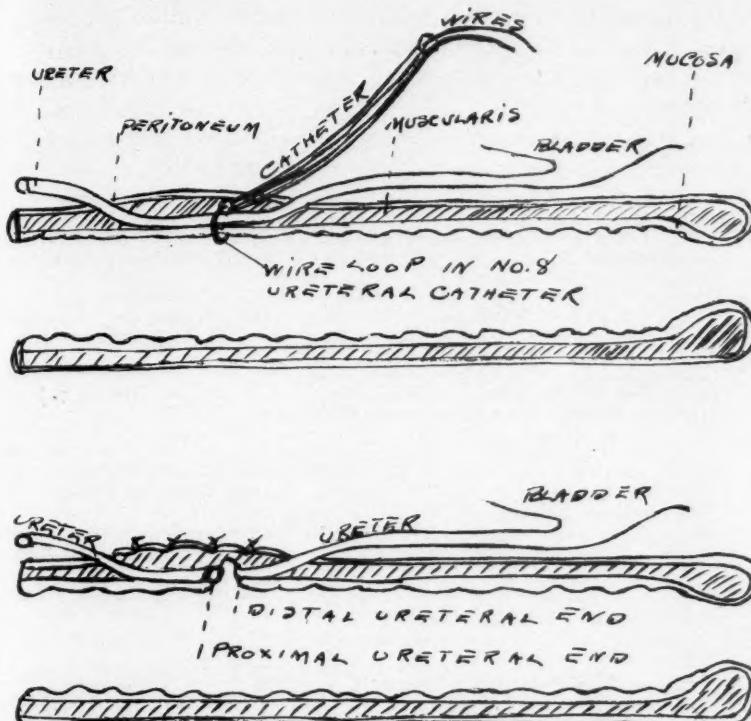


Fig. 7. Diagram illustrating No. 8 ureteral catheter, containing wire loop over ureter and passing transversely out between mucosa and muscularis.

My final modification of ureteral transplantation, already executed on the dog but not on the human being, to be applied in such a case as cited above, is performed as follows:

Both ureters are placed in the submucosal position, a No. 1 tonsil wire is made to pierce a fold of the intestinal mucosa and to encircle the ureter. The two ends of the wire are then passed out through a No. 8 ureteral rubber catheter, which catheter in turn is passed for a short distance between the muscularis and mucosa. With the incision in the gut closed and the catheter passing out extraperitoneally through a small wound in the flank and guarded by a Penrose drain, the wire and catheter is left in this position until the eighth to tenth day, when a very high and quick electro-cutting current is applied to the wire and the ureter severed. First one ureter is cut and then the other, each step being followed by intravenous urography.

If the ureters are satisfactorily disposed of, total cystectomy is easy in (a) exstrophy and, with the aid of electro-cutting and coagulation, not particularly difficult in (b) vesicovaginal fistula, (c) cer-

tain groups of patients with chronic interstitial cystitis, (d) tuberculous cystitis, with marked diminution of bladder capacity and severe pain, and (e) carcinoma of the bladder in a selected group of cases.

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THE SURGICAL TREATMENT OF HYPERTENSION

CHALMERS HALE MOORE, M. D.

Birmingham

OUR present concept of essential hypertension is that it is a dysfunction of the neurogenic endocrine vascular mechanism. The secretions of the pituitary, thyroid and adrenals play an important part in the maintenance of normal vascular tone. The autonomic nervous system occupies an important role in this function through the secretion of sympathin, and in addition acts as a regulating influence on this mechanism through the transmission of stimuli, either physical or emotional in origin.

Essential hypertension is manifested in an individual by the presence of a blood pressure that is persistently above normal limits and that from an emotional or physical stimulus will ascend to extreme heights. This condition has been observed in young children, is not rare in young adults, but is most frequently encountered in the fourth and fifth decades of life. The chief etiologic factor is probably the inheritance of a faulty autonomic nervous system. In other instances excessive mental and physical strain may be the cause of over stimulation of this regulating mechanism, setting off recurring periods of vasoconstriction over a wide area of the vascular tree. This spasm of the retinal vessels has been observed, and it was noted by Wagener that the degree of spasm corresponded closely to the stage of the disease.

The ultimate response to this excessive recurring vasoconstriction is an increase in the production of connective tissue in the arterioles of the brain, the heart and the kidneys. This sclerosing effect in the retinal arteries is manifested by the fact that as the condition progresses the variation in the caliber of the vessels due to alternate constriction and relaxation, is finally lost, and replaced by a permanent narrowing, fixation and tortuosity. It is only reasonable to assume from this observation that similar changes occur in the small arteries in the remaining portion of the arterial system.

With this picture in mind it is easy to understand the sequence of events that may follow, cerebral vasospasm and sclerosis, coronary spasm and sclerosis, chronic arteriosclerotic nephritis and general arteriosclerosis. *These conditions are the end-result of essential hypertension and not the cause of it.*

Arteriosclerosis may develop from other causes resulting in cerebral and cardiorenal changes. One observes frequently at autopsy

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advanced vascular changes in the cerebral vessels, calcification and rupture, without demonstrable hypertension during life, and in comparatively young people.

Also, not to be confused with essential hypertension is that group of individuals whose blood pressure maintains persistent high levels due to disease of the thyroid, pituitary, adrenals and to eclampsia. These fortunately are relieved by appropriate surgical measures, or in the case of basophilism by deep therapy directed at the pituitary gland.

Still another group of conditions are productive of hypertension, namely, arteriovenous aneurysm, coarctation of the aorta and glomerulonephritis. In these, obviously, the autonomic system can play no part, and surgical therapy has no place except in certain of the aneurysms.

With this brief outline of the etiologic factors involved and the resulting pathologic changes, the symptomatic pattern that follows is entirely logical. For some time the patient may be unaware of his condition until it is accidentally discovered. Many cases are now being found due to the policy of large employers of labor of examining applicants for employment, and in the course of life insurance examinations. The progress of the condition follows a fairly definite course, the only variation being the rapidity with which the symptoms develop. A certain classification may be based on this progression. The early benign group, as a rule, occurs between the fortieth and fiftieth years and requires ten to fifteen years to terminate life. In the early stages recurring headaches are complained of and careful ophthalmologic examination will reveal spasm of the retinal vessels. There is a persistent elevation of the blood pressure which may rise 50 to 100 mm. on emotional or physical stimulation.

The next group is designated as early malignant and develops more rapidly. This group may originate between the sixteenth and fiftieth years but has been seen in a child 6 years of age. It terminates fatally in four to five years.

True malignant hypertension occurs during the same years as the early benign group but progresses with great rapidity, producing death in eighteen months to two years.

As a matter of fact, any classification has to be arbitrary. The distinguishing difference in the various groups is only in the time required before the inevitable fatal ending. The symptomatic sequence is then dependent on the rapidity of progress of the organic vascular and tissue changes in the brain, heart and kidneys, mani-

fested by headache, precordial pain, myocardial failure, chronic nephritis, retinal hemorrhages, papilledema, cerebral hemorrhage and death.

The widespread incidence and 100 per cent mortality in this disease, proven statistically and admitted by our medical colleagues, has stimulated surgical thought to search for a possible solution. It is entirely too early to evaluate finally the methods of treatment that have emanated from these efforts, but certainly definite progress has been made during the recent past.

The problem that presented itself to surgery was to intercept the vasoconstrictor impulses, transmitted by the autonomic system, to a wide enough area of the arterial tree to prevent an elevation in blood pressure. In 1921, Jean, in Paris, severed the splanchnic nerves for the relief of pylorospasm. Danielopolu observed that as a result of the handling of these nerves during this procedure the blood pressure immediately rose to tremendous heights; whereas, when they were sectioned there was an immediate drop in the pressure.

Crile made the significant observation that if the region of the celiac ganglion was flooded with novocain not only was the rise in blood pressure incident to manipulation prevented but that there was a marked drop. This fact, together with his studies of the comparative anatomy and physiology of the celiac ganglia in animals prompted him to excise the celiac ganglia for the treatment of hypertension. Of his results you have already heard.

In 1925 Adson performed bilateral lumbar sympathectomy for hypertension and obtained no result. This procedure was doomed to failure because it could not have produced vasodilatation over a wide enough area. Interest was not again centered on this problem at his clinic until 1930, when by a much more radical procedure a phenomenal drop was obtained. This consisted in a laminectomy from the sixth dorsal to second lumbar vertebrae inclusive, and section of the corresponding anterior nerve roots. On account of the radical nature of this procedure it was not continued, but instead Adson and Craig developed a subdiaphragmatic approach to the splanchnic nerves. Through this approach the splanchnic nerve may be sectioned, the celiac ganglion excised and the first two lumbar ganglia and their intervening trunk removed. This produces a wide area of vasodilatation over the splanchnic vessels, denerves the adrenals and increases the blood flow through the kidneys. The procedure is done first on one side through a lumbar approach, and ten to twelve days later is repeated on the opposite side. About four weeks hospitalization is necessary.

The intelligent selection of patients to whom surgical efforts might be wisely recommended implies a careful consideration of the character of the symptoms, the rate of progress of the symptoms, the failure of response to adequate medical treatment, the age of the patient, the amount of tissue damage already present and the response to the cold pressor test.

This latter is a simple measure intended to determine the response of the blood pressure or peripheral vasoconstriction to physical stimulus. It consists of plunging the patient's hand up to the wrist in water cooled to 4 degrees C., after first having obtained the basal pressure. After plunging the hand in the cold water the blood pressure reading is taken in 30 seconds, which allows usually the maximum response. There should be a return to the previous reading in 4 to 8 minutes. The sudden rise in an essential hypertensive patient may be from 30 to 100 mm., while in a normal individual rarely more than a 10 or 20 mm. rise is noted. This test is indicative of the fact that the arterioles retain their elasticity and it acts as a good measuring rod of one's therapeutic efforts. It is my opinion that when this response is obtained, surgery is indicated, because it has been shown that the arterioles still retain their elasticity and contractile power. The primary object of the surgical treatment is to prevent the vasoconstriction that this test proves to be present. The rigid selection of cases makes for better statistics, but careful analysis of the work of others of greater experience, as well as my own observations during the past two years, leaves me with the feeling that until the value of surgical treatment is finally established there is some question as to whether any case should be refused the benefit of operation in which any elasticity remains in the vessel walls. At the Mayo Clinic operation is advised only for patients whose pressure responds favorably to the intermittent, intravenous injection of pentothal, or to sodium amytal or to sodium nitrite. It is felt then that if there is an inadequate response to these measures operation will almost certainly result in failure. It is useless to intercept the vasoconstrictor mechanism when the vessels have lost their ability to dilate due to fixed, sclerotic walls. Marked renal insufficiency and congestive heart failure contraindicate operation.

It should be emphasized that every case of essential hypertension at some period during its development will respond to surgical treatment. It should be stated with equal emphasis that beyond a certain point operation will be a complete failure and only serve to throw an otherwise valuable procedure into disrepute. Nowhere is sound judgment more necessary than in the selection of patients who may be advised to submit to surgery for hypertension.

As to the results of operation the time has already come when one can say at least that the improvement obtained justifies continued trial of the procedure if rigid selectivity of cases is strictly observed. The risk involved is slight when operation is performed by experienced hands. In my own series of 22 cases during a period of thirty months the following statistics develop:

ANALYSIS OF 22 CASES	Cases	%
Immediate postoperative drop in B. P.....	20	90
Reduction in B. P. maintained 1 year or over.....	10	45
Symptomatic improvement—No reduction in B. P....	6	27
No improvement—No reduction (except immediate) ..	6	27
Not even immediate postoperative reduction in B. P... .	2	9
Deaths—result of operation.....	1	4

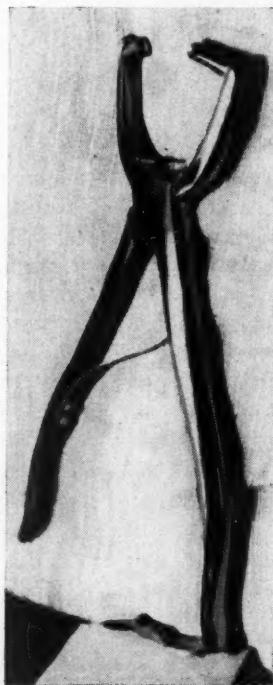
Attention should be called particularly to that group in which symptomatic improvement was obtained but in which there was no sustained drop in pressure. It is quite remarkable how many of these people are delighted at the improvement in the way they actually feel, while the systolic and diastolic pressures are almost identical with their preoperative readings. It has been observed in this group, however, that they do not give the same response to the cold pressor test following operation, the reaction approaching normal. This indicates that the constrictor impulses have been intercepted and that while the pressure level runs along about the same as before, there at least has been an effective cushioning of shocks to sudden stimuli and a cerebral vascular hemorrhage may be prevented for a long period of time, prolonging possibly a period of useful activity to a valuable individual or beloved member of a family. These factors, I think, are worthy of your careful consideration.

USEFUL BONE FORCEPS

G. A. HENDON, M. D.

Louisville

The forceps herein illustrated and described possess certain advantages which should recommend it to the attention of surgeons who use instruments of this type. The principal advantage is that it can be made to fish out and lift firmly a deeply imbedded fragment of bone while doing no damage to the bone.



It is incapable of inflicting injury because its two incisors are blunt and must project beyond an object before they will engage or come together. I have named this The Clevis Forceps. The parallel levers which constitute the upper and lower jaws are curved to accommodate the larger long bones. The handles are provided at their proximal extremities with an automatic locking device so the grasp of the forceps can be secured after engaging. I have found it of great value in exteriorizing the deeply imbedded fragments of bone so they can be trimmed or sawed smooth for accurate approximation.

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INTERDEPENDENCE OF SURGEON AND INTERNIST

The great difference between surgeons and those who practice internal medicine, as I see it, is that you are able to do things with your hands and can many times feel that you have by your own efforts effected a cure, whereas, except in a few instances where specifics are available, the internist must be content with making a diagnosis and ameliorating symptoms until the forces of nature produce a cure or, as in so many cases, unfortunately, the disease progresses to a fatal termination.

Both branches of the medical art have made tremendous strides within the past two or three decades. The evolution of surgery is nothing short of miraculous. One by one the treatment of diseases that were once thought to be purely medical has been taken over by the surgeons to a greater or less extent.

It is true that attempts to treat nephritis by decapsulation of the kidney are no longer made, nor do the surgeons get a chance to take the spleens out of our patients with pernicious anemia. But a few years ago it would have taken a lot of imagination to predict that the surgeon would ever be called in to operate for adhesive peri-

Read before the Postgraduate Surgical Assembly, the ninth annual meeting, of The Southeastern Surgical Congress, Louisville, March 7, 8 and 9, 1938.

carditis, arterial hypertension or angina pectoris. Pulmonary tuberculosis was for years a medical stronghold, but now the tuberculosis sanitorium is no longer a safe retreat from the influence of the surgeon, since the advent of operations upon the phrenic nerve, thoracoplasties and, more recently, lobectomies.

Thirty years ago a surgeon was almost always a man who, having practiced medicine for years and having begun to take up surgery as a matter of local necessity or from a natural inclination, finally had developed into what was then called a surgeon. At that time every surgeon was his own medical man, he made his diagnosis largely alone, decided upon the preoperative and the postoperative care of patients and rarely called in his medical confreres for advice. As the complexities of surgery grew and as medical knowledge extended, it became almost impossible for one man to have the intimate knowledge of both great departments of medicine, so that now we find the majority of surgeons relying on some medical associate for advice concerning problems that are not strictly surgical.

The value of surgeons to the community and to the internist is self-evident, for where would the medical man be after diagnosing a surgical condition if the surgeon were not available to correct it? However, very often there are other things to consider besides the operation. Some of these conditions call for medical advice. The surgical mind is not always fitted for that painstaking attention to certain details that should be the every day experience of those engaged in internal medicine. I do not mean by this that many surgeons are not capable of diagnosing and treating medical conditions. In deciding whether to operate, the good surgeon is in no more of a hurry than is his medical advisor. In fact, the opposite may be the case, for often the internist feels that an immediate operation is necessary when the surgeon, having a deeper realization of the risk and having to assume the responsibility as well, will advise watchful waiting, and in many cases time proves that the surgeon is right. However, there are certain medical conditions which resemble surgical ones so closely that a partnership diagnosis and opinion is better than that of either the surgeon or the internist alone.

It is hardly necessary to mention these conditions. You surgeons all know them very well. Pneumonia or typhoid fever simulating appendicitis, gastric crises of tabes and coronary disease resembling acute abdominal conditions; a neurosis of any organ in the abdomen having the appearance of organic disease—some of these are easy to differentiate if thought of, but others like coronary disease may be extremely difficult. Only within the past week I have seen two cases of diaphragmatic pleurisy, each of which could easily have been mis-

taken for a ruptured duodenal ulcer. The pain of gallbladder disease and coronary occlusion may so closely resemble each other at times that the decision cannot be made even by resorting to the x-ray and the electrocardiograph. A very painstaking study by both surgeon and internist is certainly necessary here to avoid a mistake. Usually it is the medical man who must locate the empyema or the lung abscess, diagnose perforations in typhoid fever and suspect gallbladder or stomach disease. Indeed it is seldom that any disease of the gastrointestinal tract is seen first by the surgeon. However, it is the surgeon who has called attention to the fact that cancer of the stomach and pernicious anemia must be differentiated early and that any severe anemia may be due to cancer of the colon.

After a diagnosis is made and an operation decided upon the internist is often called upon to pass judgment upon the circulatory or respiratory systems. In deciding whether a heart is adequate to meet the demands put upon it by a general anesthetic, it has been my experience that where the heart meets without difficulty the ordinary demands placed on it, there is usually little danger. More important than the physical examination of the heart itself is the cardiac history of the patient, whether there have been symptoms of inadequacy on the part of the heart to meet moderate exertion, and especially important whether there have been symptoms of coronary disease previously. The blood pressure readings may also influence the choice of anesthetics, since some forms of anesthesia lower blood pressure, while the stage of excitement with others may cause such a rise as to be dangerous to the hypertensive. It may be necessary to decide whether a patient needs digitalis, and if so, the digitalization of this individual should be in the hands of the internist. Conditions in the lungs and respiratory tract also have great influence in deciding whether a general anesthetic is safe. The specialist in internal medicine should be able to advise in regard to them.

Not only before but after operation the internist can be of great assistance to the surgeon. In postoperative treatment I think that at times the surgeon is a little likely to follow a routine, when individualization is more necessary. The giving of large amounts of saline and glucose I have no doubt has saved many lives, but on the other hand there are patients who cannot excrete these enormous amounts of fluids and become waterlogged. Intelligent medical care may prevent some mistakes here. There is a general opinion among internists that for those patients who have been submitted to operations on the gastrointestinal tract, the diet should be carefully supervised for a much longer time than is usually done. The final success or failure of an operation may rest upon this postoperative care.

All surgeons now turn to the internist when diabetic patients are to be operated upon, since the management of the surgical diabetic is a highly specialized one. The utmost care must be taken to prevent acidosis and coma. The necessity for giving adequate amounts of carbohydrate buffered by insulin when required is sometimes overlooked. Indeed in the past I have seen orders written by a surgeon and I am sorry to say at times by a medical man, specifying simply "a diabetic diet" or a "low carbohydrate diet." Once I saw an order written for a diabetic patient which said "no carbohydrates" or "no starchy foods." If insulin is required, remember that its management is not always simple—no general rules will fit all cases. Experience is needed to handle it intelligently, and each patient should be an individual problem.

The urologic surgeons have taught us all what preoperative care will accomplish in taking care of patients whose kidney function has been impaired. The time may come when just as much attention will be paid to the liver function and appropriate steps, some of which are already known, will be taken to prevent failure of this organ.

The internist should be very grateful to the surgeon for many things. You not only have made it possible to "do something" after a diagnosis is made, but you have also helped make a correct pre-operative diagnosis possible by operating often enough to fix the criteria upon which such a diagnosis can be based. Then too, you have rendered great service to the medical profession in a business way: you have made the public understand that a doctor's services are worth more than so much per visit.

It has been hard to teach the public that the value of the physician's services in treating a medical case does not depend upon the amount of time spent with the patient nor upon the number of visits. By the best of modern methods in favorable cases, illness is much shortened and the compensation of the doctor should be greater than if the patient were sick for a longer time. With the example of the surgeons before us the internists may in time get more adequate remuneration for their services.

The modern evaluation of the physician and surgeon shows a great change since ancient days when surgery was an outcast in medical practice and was given over to the barbers. In England even today the surgeon is called Mister. I am afraid that now sometimes surgeons look down on the internists much as the physicians used to look down on the barbers. This should not be the case, for it seems to me that the two main branches of medicine are equally important. Each must depend for support upon the other. That this is coming to pass is shown by the fact that controversies over treatment are

becoming fewer and fewer. To cite just one example: you remember the war that was waged for so long a time over the treatment of duodenal ulcer. The surgeon claimed that the condition always demanded operation while the internist was reluctant to give in to this idea. Now the surgeons and internists are in complete agreement upon the treatment and the indications for surgical intervention.

Very few patients can be said to be purely surgical or purely medical. There are medical aspects to the majority of surgical conditions and there are few medical patients who will not require surgical attention or advice. This being the case, in this paper I have tried to hint at a few of the ways in which an internist can be of help to the surgeon.

Since it is impossible that a surgeon can know all of medicine or an internist have more than a working knowledge of surgery, it would seem to be for the best interests of the patient that these two—surgeon and internist—should more and more work in co-operation.

ERNEST B. BRADLEY, M. D.

Lexington, Ky.

BOOK REVIEWS

The Editors of THE SOUTHERN SURGEON will at all times welcome new books in the field of surgery and will acknowledge their receipt in these pages. The Editors do not, however, agree to review all books that have been submitted without solicitation.

SURGICAL DISEASES OF THE MOUTH AND JAWS. By EARL CALVIN PADGETT, B. S., M. D., F. A. C. S., Associate Professor of Clinical Surgery, University of Kansas School of Medicine, Kansas City, Kansas; Associate Professor of Oral Surgery, Kansas City Western Dental College, Kansas City, Missouri. 807 pages, with 334 illustrations. Price, \$10. Philadelphia and London: W. B. Saunders Company, 1938.

The mouth and jaws constitute a border ground between surgery and dentistry. The dentist, as a very highly specialized surgeon, can for example sometimes handle a fracture of the maxilla or mandible better than a physician. And the surgeon sometimes has to extract a tooth in treating a tumor of the jaw or osteomyelitis. The dentist spends more time in the study of the oral cavities of his patients and in this day and age he cannot be content to notice only the teeth. He must be on the alert in particular to recognize early cancer of the buccal cavity.

Dr. Padgett has produced an encyclopediac work. He has written an excellent account of the pathology of the region. Chapters are also devoted to wounds and other injuries, to fractures and dislocations, inflammatory conditions, and diseases involving not only the mouth and the pharynx but also the antrum and neck; neuralgias, congenital defects, benign and malignant tumors are also considered.

The plastic surgeon as well as the dental surgeon will find this work of constant value. The otorhinolaryngologist will often find in it information he needs. The general surgeon will find help in handling cancer of the buccal cavity or cellulitis of the neck. Even the medical man who confines his work to diagnosis can find help. In short, this is a splendid book, one that every doctor will need more or less constantly.

TREATMENT IN GENERAL PRACTICE. By HARRY BECKMAN, M. D., Professor of Pharmacology at Marquette University School of Medicine, Milwaukee, Wis. Third Edition, Revised and Entirely Reset. 787 pages. Price, \$10. Philadelphia and London: W. B. Saunders Company, 1938.

On the whole one of the most valuable books that has been published in the twentieth century is Beckman's Treatment. With it only for reference, a doctor could practice good, modern medicine—not the very best perhaps, not a type to include obstetrics or surgery or any of its specialties, but still a better grade of medicine than many men exhibit now.

The new edition is a masterpiece of revision. Many matters that were still controversial at the time of earlier ones have been settled, and other arguments have been condensed, so a great deal of new material has been introduced without increasing the size of the book. Several subjects which this reviewer has been studying intensely are absolutely A-1 in the new work. While covering a wide field, Dr. Beckman has succeeded in writing clearly and concisely and at the same time conversationally.

However earnestly a surgeon may desire to limit his activities to strictly surgical procedures, he must at times pay attention to his patients' minor ills and he should therefore find this book indispensable.

ATHLETIC INJURIES: PREVENTION, DIAGNOSIS AND TREATMENT. By AUGUSTUS THORNDIKE, JR., M. D., Surgeon in the Department of Hygiene, Harvard University; Assistant in Surgery, Harvard Medical School; Associate Surgeon, Children's Hospital, Boston, Massachusetts. 208 pages, with 104 illustrations. Price, \$3. Philadelphia: Lea & Febiger, 1938.

This excellent pocket-sized book, based primarily upon a study of all injuries incurred in athletics at Harvard over a period of six years, should be carefully studied by everyone who may be responsible for the care of injuries to young athletes. Because fractures incurred by them are no different from those incurred by less romantic persons and because there are a number of excellent standard textbooks on fractures, the treatment of fractures is not detailed. Otherwise the discussion is complete.

A famous coach in this part of the country boasts that he has been responsible for the sale of no less than fifty copies and it would be desirable for every other coach and trainer, as well as every school physician, to acquire one.

The work is of general interest on account of its exposition of the physiologic research that has been done on athletes. The only adverse criticism is a note of surprise that in a publication from Harvard University should appear repeatedly the word "preventative."

THE SURGICAL TREATMENT OF HYPERTENSION. By GEORGE CRILE, M. D. Edited by Amy Rowland. 239 pages, with 52 illustrations. Price, \$4. Philadelphia and London: W. B. Saunders Company, 1938.

As Dr. Bradley remarks elsewhere in this issue, the surgeon is constantly making inroads into domains once considered exclusively medical. One of the most startling of these invasions is in the treatment of hypertension, and this, because of frequent failures by the medical regimen, is now unquestionably one of the liveliest subjects before us.

Dr. Crile was the pioneer in this field: his first operation for the control of hypertension was performed back in 1914. In the intervening years, as a result of clinical experience, operations and collateral research, from time to time he has altered his plan of attack. While on his expedition into Africa, he concluded that the celiac ganglion was the key to the situation. Fierce, active animals like the lion have large celiac ganglia, while sluggish ones like the alligator, docile ones like the sheep have small ganglia. Hyperkinetic, hypertensive human beings tend to have inordinately large celiac ganglia: it therefore appeared logical to remove them as a therapeutic measure. Just after his return from Africa in 1936 he made the first public exposition of this thesis before the New Orleans Assembly of The Southeastern Surgical Congress, and he presented his results at the Louisville meeting. Readers of *THE SOUTHERN SURGEON* will also recall several short papers in these pages.

Now that Dr. Crile has operated on the celiac ganglion in 148 cases it is most interesting to have his outline of the whole subject, including his description of the technic of the operation. It is astounding that his operative mortality is less than 3 per cent. One wonders if any other surgeon could match his superb skill.

The magic of Dr. Crile's personality must make one share his enthusiasms, but on seeing his work in cold print the skeptic will wonder if he has solved the problem of hypertension because of two reasons. The first is that only sixteen patients have been followed for more than a year after bilateral celiac ganglionectomy. The second cannot be better expressed than in his own words:

"We must at once guard against the inference that the presence of large celiac ganglia and a large sympathetic complex means that hypertension will inevitably develop. No matter how powerful the equipment for crisis energy, if it is governed properly by the brain—by reason, by discipline, whether the discipline be from religion or philosophy or some social sense—then vigorous old age may be reached without the occurrence of essential hypertension."

This book however provokes thought and it may prove to mark an epoch. Keep your copy of the first edition: some day it may be worth a young fortune.

A SYNOPSIS OF THE DIAGNOSIS OF THE ACUTE SURGICAL DISEASES OF THE ABDOMEN. By JOHN A. HARDY, B. Sc., M. D., F. A. C. S., El Paso, Texas. 345 pages, with 92 illustrations. Price, \$4.50. St. Louis: The C. V. Mosby Company, 1938.

Some authors of modern textbooks on surgical diagnosis seem to believe that it is only necessary for the surgeon to be an interpreter of laboratory reports. Dr. Hardy, on the other hand, believes that the surgeon should be primarily a man of brains. He has simplified for him the use of his brains by outlining differential diagnosis in the fewest possible words and it is needless to say that this includes the indications for laboratory aid.

Perhaps the opus is presented in pocket-size because intended for house officers. Its small compass has necessitated type which will not increase its value to the presbyopic.

A PRIMER FOR DIABETIC PATIENTS. By RUSSELL M. WILDER, M. D., Ph. D., F. A. C. P., The Mayo Clinic, etc. Sixth edition. Reset. 191 pages. Price, \$1.75. Philadelphia and London: W. B. Saunders Company, 1937.

The discovery of insulin made previous books on diabetes out of date; just so, though to a less extent, protamine zinc insulinate has outmoded the diabetic manuals of three years ago. The new Wilder carries on the excellent traditions of the five earlier editions, and again reminds the patient that the primer is in no sense a substitute for the supervision of a physician.

A TEXTBOOK OF OPHTHALMOLOGY. By SANFORD R. GIFFORD, M. A., M. D., F. A. C. S., Professor of Ophthalmology, Northwestern University Medical School, Chicago; Attending Ophthalmologist, Passavant Memorial, Cook County, Wesley Memorial and Evanston Hospitals. 492 pages, with 249 illustrations. Price, \$4. Philadelphia and London: W. B. Saunders Company, 1938.

For the undergraduate and for the man who has been in general practice for a number of years, this profusely illustrated handbook of ophthalmology should prove valuable.

Review of Neoplasms

formerly

The Review of Tumor Therapy

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THE SURGERY OF CARCINOMA OF THE BREAST

The breast is undoubtedly one of the most favorable locations for the cure of cancer. The indications for surgical treatment are so well established that the subject seems almost a closed book. Yet advances continue to be made and the issues involved are still so alive that Trout chose Carcinoma of the Breast as the subject for his Chairman's Address before the Section on Surgery at the recent meeting of the American Medical Association in San Francisco.

The most important factors in the prognosis of breast cancer are the duration of the disease and extension of the growth at the time of operation. Davis¹ found 75 per cent cures in cases where symptoms had been present for less than six months and only 25 per cent for cases of longer duration. Cathcart² reported 64 per cent cures among private patients as contrasted with 45 per cent for cases in a charity hospital. The well-known fact that the presence of axillary involvement markedly decreases the number of five year cures is borne out by the recent figures of Davis¹ and Pfahler³.

As aids to earlier diagnosis two relatively new procedures are described. Scott⁴ employs his shadow test to demonstrate early changes in the skin overlying a carcinoma. The test consists of obliquely illuminating the breast surface with a flashlight in a darkened room as the breast is manipulated. This simple method has enabled Scott to recognize the skin changes in breast cancer before gross dimpling has occurred, and in one case even without a palpable mass. Hicken, Best, Hunt, and Harris⁵ reported the results of roentgen visualization of the breast; 625 mammograms were made after either the injection of radio-opaque materials into the milk ducts or the insufflation of carbon dioxide gas into the surrounding matrix. Conditions other than cancer may produce skin changes in the breast. For example Coleman⁶ describes two cases of circumscribed scleroderma simulating breast carcinoma. In neither of these cases was a palpable mass present.

The value of irradiation as an adjunct to surgery is indicated by the figures of Pfahler³, Keynes⁷, Bade and Baden⁸, and Hintze⁹. The improvement in the number of five year cures had been particularly striking in cases with extension to the axilla or elsewhere. Pfahler and Vastine¹⁰ state that various statistics show 11 to 73 per cent improvement with postoperative irradiation over operation alone. It is their belief that skilful preoperative irradiation, then skilful operation, followed by skilful postoperative irradiation should double the total number of persons with cancer of the breast well after five years. They further advise that, since postoperative irradiation does not interfere with wound healing, treatment should be started as early as possible, that is within ten days to two weeks after operation.

The routine of preoperative irradiation remains an open one until more results are reported. Pfahler³ presents the evidence for its value especially in stage two where axillary extension is present. O'Brien¹¹ in advising preoperative treatment notes that the appearance time of skin metastases was in direct relation to the extent of the growth at the time of operation. O'Brien reported 21 per cent of recurrent skin nodules in cases irradiated postoperatively, Kress¹² also mentions the use of preoperative radiation.

The many recent studies on the relation of ovarian and other hormones to breast carcinoma are too extensive to review here. However, from a practical standpoint it would seem advisable to avoid subsequent pregnancies after amputation of the breast for cancer as recommended by Harrington¹³ and by Seebohm¹⁴. Pfahler and Vastine advise ovarian sterilization for all patients still menstruating. Koerbler¹⁵ believes that the artificial interruption both of pregnancy and lactation may play a role in producing changes in the breast that lead to malignancy.

The possible relation between chronic cystic mastitis and carcinoma of the breast is receiving less support than formerly. Lewis and Geschickter¹⁶ found only four patients who died of breast carcinoma among 1,048 cases of chronic cystic mastitis. Likewise 2,675 specimens of carcinoma showed the changes of Schimmellbusch's disease in only 0.5 per cent of cases. On the other hand the comparatively infrequent form of comedo or duct carcinoma did show histologically a relation to adenosis in 30 per cent of cases. Lewis and Geschickter¹⁷ report in another paper that comedo carcinoma grows slowly, metastasizes late and offers the best chance of cure (85 per cent) of all forms of breast cancer. They recommend that, since cystic diseases and adenosis are not precancerous lesions, radical operations should not be performed as frequently as they are.

Herzog¹⁸ believed his histologic studies demonstrated a relationship between the comparatively benign and slowly growing colloid carcinoma and chronic cystic disease. Wanke¹⁹ avoids operation if biopsy proves that the lesion is chronic cystic mastitis, since he believes that the condition carries little risk of subsequent malignancy. Most of us will continue to take the position that a woman with a lumpy breast may also have cancer and that any suspicious single mass must be examined histologically before the possibility of carcinoma can be ruled out.

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PREOPERATIVE AND PRE-RADIUM ROENTGEN THERAPY

For many years roentgen therapy has been used in the postoperative treatment of proven carcinoma of the breast. Its efficacy for this purpose is well recognized. In a similar way, roentgen therapy has been used after primary application of radium to carcinoma of the uterine cervix.

There has developed a growing tendency, in more recent years, toward preoperative roentgen therapy in breast carcinoma and pre-radium roentgen therapy in carcinoma of the uterine cervix. It is not to be implied that these will replace the former methods entirely, but that combinations are often indicated, and these newer methods are also useful in other forms of carcinoma. Stebbing⁵, Levitt⁴, Cohn² and Adair¹ all state in recent articles that they believe preoperative therapy should not be limited to these fields; they are convinced that if such methods are used more generally in the treatment of other malignant lesions of somewhat similar nature and course, more permanent cures will be obtained.

The fundamental purpose of the operation for breast carcinoma is the removal of all the primary growth and the evident axillary metastases. The surgeon tries to remove as much of the tissues which contain cancerous cells as is feasible. He can and does remove those glands and groups of cancer cells which are definitely visible or palpable. The operative limitations do not allow him to remove all of the surrounding tissue which may contain cancer cells. In cutting through the neighboring tissues, he may spread cancer cells in the line of the incision, and it is fairly common to see recurrences there in spite of adequate postoperative irradiation.

Before beginning the operation, the surgeon insists upon thorough cleansing of the skin, and sterilization of it with one or several antiseptic fluids. No attempt is made to sterilize the underlying tissues from the standpoint of free malignant cells which may be present. No matter how carefully the physical examination has been conducted in regard to the presence or absence of palpable masses, a certain number of cases with preoperative microscopic metastases, neither palpable or visible, will be missed. The author has seen cases of breast carcinoma with no palpable tumor in the breast, but positive axillary and distant metastases.

It does seem reasonable to prepare the underlying tissues for the operation just as well as to prepare the skin. In other words, with adequate preoperative roentgen therapy, many of these microscopic cancer cells would be destroyed, and the chances of leaving them

behind or of spreading them by operative procedures would be greatly reduced.

In certain of the more advanced cases of carcinoma of the breast, adequate roentgen therapy may change an inoperable carcinoma into an operable one. I do not believe that there is a great improvement in the ultimate prognosis in such cases, but if they can be brought to a position where simple amputation of the breast is feasible, the large, ulcerated, infected mass may be removed, and the miserable existence of the unfortunate individual is made more bearable. Cohn² states the prognosis of all such cases is greatly improved by preoperative therapy, and in some cases complete cures for five years and longer have been obtained.

Some objections to preoperative roentgen therapy have been given, such as: that the operation is unduly delayed; that there may be interference with healing after operation; that there may be deep extensions during the period of irradiation; and that the operation is made more difficult.

I have seen no evidence of extension of the malignancy during the course of preoperative irradiation, and can find no reports of such in the literature. Almost invariably there is a marked regression so the delay in operation should not cause alarm. If adequate time is allowed for the radiation reaction to subside and the total dosage used is not too great, interference with healing will rarely be encountered, and the operation is often made simpler rather than more complex.

It must be remembered that, if deep extensions have occurred or are occurring, operation and postoperative irradiation over abnormal tissues are not more apt to control them than preoperative radiation. It seems more logical that preoperative radiation into more nearly normal surrounding tissues, will be more apt to control deep extensions and at the same time destroy or attenuate the more superficial parts of the growth.

Adair¹, Cohn² and Levitt⁴ all agree that adequate preoperative irradiation does not increase the difficulty of operation in most cases. They believe that in many a procedure less radical than the classical resection is often justified. The preoperative radiation should be fairly intense, and sufficient time should be allowed (usually not less than six weeks) for the radiation effects to be completed before operation is attempted.

During the years when radical surgery was considered the method of choice in the treatment of carcinoma of the uterine cervix, over 40 per cent of the earliest cases showed microscopic metastases in

the parametria. In those patients in whom the disease had advanced beyond the early stages, this percentage mounted rapidly toward 100. Most surgeons have abandoned hysterectomy in favor of irradiation in the treatment of this disease. The most frequently followed method, up to recent years, has been the use of primary application of radium to the cervix, followed by roentgen irradiation to the pelvis. Excellent results may be obtained by this method in the early cases, but there are other points to be considered in the later cases.

In these more advanced lesions there is, in addition to the microscopic and macroscopic parametrial metastases, a certain amount of infection with dilated lymphatic and venous channels. It has been shown that radium is not well tolerated and cannot properly affect cancer cells in an infected field. On the other hand, Coutard^a and others have recently shown that roentgen rays directed over the pelvis, with proper intensity and total dosage, will clean up these parametrial invasions and infections. By crossfiring through the pelvis, the cervix receives the greatest amount of irradiation, and the primary growth is reduced, often obliterated. The cervix is then clean, and the parametria are freed from infiltration and infection. A moderate dosage of radium can then be applied to destroy effectively the residual cancer cells.

Other reasons for applying roentgen irradiation before radium in these cases have been stated in the literature. Some investigators believe that primary radium applications in advanced cervical carcinoma tend to drive cancer cells into the parametria. This may be due to the swelling of the tissues, both from infection and the action of the radium, so that lymph and venous channels are opened up allowing attenuated or partially attenuated cells to migrate outward. If by thorough roentgen irradiation, these channels can be reduced in size or closed off, the chance of cells wandering out is reduced. In addition, the factor of distance is very important in radium applications. It is well known that the effectiveness of any radium applicator in the cervix is largely limited to the tissue within 2 cm. of it. The primary growth may be limited to this area, but the secondary portion, the part which will eventually kill the patient, is not limited to this area. If one can stop the spread of the growth, clean up the pelvic infection and reduce the activity, ulceration and infection of the primary growth, he can improve markedly the ultimate effect of radium implanted in the cervix.

These are the reasons why I believe that preoperative roentgen therapy in carcinoma of the breast, and pre-radium roentgen therapy in advanced carcinoma of the uterine cervix are definitely indi-

cated. I reiterate that these therapeutic measures should not be limited to the specific types of carcinoma mentioned. They are definitely indicated in many other types of malignant lesions elsewhere in the body. The same reasons and principles for application of them in these specific instances, may well apply to other lesions. It is not always enough to use postoperative roentgen therapy alone, if we are to increase the number of cures. A judicious use of pre-operative and pre-radium roentgen therapy will improve the prognosis of many types of malignancy.

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MICROSCOPIC CHANGES IN TUMORS FOLLOWING IRRADIATION

For many years great significance has been attached to the direct reaction of malignant cells to the influence of roentgen rays and radium. Recently attention has been directed to the reaction of the tumor tissue as a whole to irradiation; in other words, our viewpoint has broadened to the consideration of tissue reactions, of which the cellular reaction is but a part. Malignant tumors are complicated structures and in general are composed of neoplastic cells, whether epithelial or derivatives of mesothelial cells, connective tissue cells and fibrils forming the stroma, blood vessels, and in some instances nerves. Although the connective tissue and blood vessels are not derived from the tissue in which the neoplasm develops, they become, nevertheless, essential parts of the tumor, and the welfare of the tumor depends upon their preservation and coincident development. It therefore seems sound to insist upon the viewpoint that in tumors we are dealing with a complicated tissue and not merely with a group of proliferating cells.

While in general tumor tissue reacts similarly to roentgen rays and radium, the former is supposed to stimulate to a greater degree the vascular connective tissue response and the latter is thought to

act more directly upon the malignant cells. Nevertheless, either type of ray will produce the whole series of reactions to be described if administered in an effective manner to suitable tumors. The degree of reaction of tumor tissue parallels closely the pathologist's estimation of their ray sensitivity.

For the purposes of description the reaction of tumors to irradiation may be considered under three main headings: the direct effect of the rays upon the neoplastic cells; the reaction of the vascular connective tissue bed, with the production of a non-specific type of inflammation; and the effects accruing from the disturbances to the blood supply of the tumor due to the above mentioned processes. It must be borne in mind, however, that these processes develop more or less simultaneously, and, in fact, depend upon one another to produce the final result.

The effects upon the malignant cells are evidenced within 24 hours after the commencement of irradiation by swelling and pallor of the nuclei. This is followed by vacuolization, shrinkage, fragmentation, and lysis of nuclei. Cytoplasmic changes commence a little later than nuclear changes, and consist of swelling, loss of cell outline, and vacuolization, with final destruction of the cell. If the influences of the rays are removed during the early phases of degeneration, before the nuclei are too severely damaged, the cells may recover completely, and in time be capable of proliferation. The effect upon mitosis is quite consistent. In the first day or two after the commencement of irradiation they disappear, only to reappear in great numbers on the second or third day; however, they then exhibit great irregularities in form, and degenerate rapidly. By the fifth or sixth day mitoses have entirely disappeared, and they do not reappear with any great frequency for several weeks, although this period has not been definitely established and is probably subject to great variation even in tumors of similar type. It is of interest to note that if or when a malignant tumor recurs the subsequent generations of cells have in general the appearance possessed by the neoplastic cells before irradiation. No evidence has been produced to show that exposure to roentgen rays and radium causes any discernible, consistent anatomic alteration in the descendants of surviving neoplastic cells.

The vascular connective tissue reaction is often difficult to evaluate histologically in routine studies, because of the commonly associated inflammatory reaction produced by the tumor itself. This is particularly true of neoplasms exposed to infection, such as skin, cervical and gastrointestinal cancer, where the infection stimulates extremely active inflammatory response. Reaction to the rays is first evidenced by hyperemia and exudation of serum into the stroma.

Lymphocytes commonly appear in great numbers by the fifth day following the commencement of irradiation, and their appearance is regarded as a favorable response. Varying degrees of swelling and mucinous degeneration of the connective tissue fibrils follow. At about this period there also occurs proliferation of connective tissue and capillaries, and then the stroma has the appearance of granulation tissue. Associated with this there is an ordinary inflammatory reaction, probably stimulated by a combination of the ray effect and the presence of degenerating tissues. The end result is replacement by fibrous scar tissue. If all of the neoplastic cells are destroyed this is a favorable outcome, but if some cells persist in the scar tissue, they are then less vulnerable to subsequent irradiation, and after remaining quiescent for varying periods of time are capable of proliferating, thus producing a recurrence of the tumor.

The third factor to consider is the result of disturbance of the blood supply of the tumor. This consists of obliteration of the lumen of arteries and veins either by proliferative changes or by thrombosis. It occurs more strikingly in larger tumors, and the result is infarction. The resultant necrosis in turn stimulates an inflammatory reaction on the part of the viable tissue which further complicates the histologic picture. Whether the rays produce an actual effect upon the blood vessel walls, or whether the changes are secondary to the degenerative and inflammatory alterations resulting from irradiation, has not been established, but probably these and perhaps other unknown factors are involved.

Thus it has been shown that the destruction of neoplastic tissue following exposure to roentgen rays and radium is the result of several processes which are mutually interdependent, and occur simultaneously or in succession. The individual cellular and tissue changes represent general types of reactions to injury, and may be observed in numerous common lesions; nevertheless, the whole sequence of events is observed under no other conditions. The importance of the general tissue reaction as a factor in the destruction of irradiated tumors cannot be over emphasized. It helps to explain the fact that cells of malignant tumors are destroyed in the animal body with much less intense irradiation than is required to destroy neoplastic cells *in vitro*.

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RADIATION SKIN REACTIONS AND RECOVERY

A limiting factor to the quantity of radiation that can be applied to any area, either superficial or deep, from an external source of either x-ray or radium is the ability of the skin to survive the dose. Therefore, it is necessary to have a complete understanding of the various biologic effects of rays on the skin and in particular the so-called erythema doses. Erythema is the reaction of the superficial capillary system resulting from a localized vascular congestion and interstitial edema in the papillas and subpapillary plexuses in the corium. The erythema reaction, therefore, is not primarily a reaction of the epidermis or epithelial cells but as pointed out by Brunschwig¹ and Rost² it should be considered a mesoblastic reaction and may thus parallel the response of the stroma, tumor bed, or vascular connective tissue. This places an entirely new emphasis on the importance of observing carefully and producing exactly the erythema reaction that is indicated for the particular tumor that is being treated. As Coutard³ has repeatedly pointed out one of the main advantages in protracting treatment over many days is to produce the minimum disturbance of the vascular connective tissue bed, the sparing of which may be as necessary to combat the tumor cells as is the x-ray effect directly on the cells. We not only need to be entirely familiar with the erythema reactions to prevent overdosage of the skin with irradiation but from the type and degree of the erythema we can infer certain effects on the tumor bed.

Holznecht⁴ originally described four degrees of erythema as follows:

FIRST DEGREE. There is a latent period of as long as 3 weeks. It is characterized by transient pinkness and epilation and occasionally by the subsequent appearance of pigmentation. The skin returns entirely to normal after a fairly short period of time although the pigmentation may persist for several months.

SECOND DEGREE. The latent period is usually of less than 2 weeks. There is epilation, deep red erythema, swelling and subsequent scaling of the skin. Itching and burning sensations are frequent. In the end, the tissues return to an approximately normal condition, but at a later stage there is a liability to the occurrence of telangiectasis and atrophy.

THIRD DEGREE. To the symptoms and signs of the second degree reaction are added the formation of blisters and eroding excoriations. The erythema takes on a dull bluish-red color and the subjective symptoms are frequently very pronounced. Healing may occur without any permanent damage to the skin but frequently there is a complete destruction of the oil and sweat glands and hair follicles.

FOURTH DEGREE. This has a latent period of only a few days and deep ulcers usually follow the earlier reactions. Healing, of course, is remarkably slow and may not occur.

There has lately appeared in the literature new names for these old reactions. The threshold erythema of Quimby is the same reaction as the first degree Holznecht. Quimby had defined it as the amount of radiation necessary to produce a just appreciable reddening of the skin of 80 per cent of patients. About 525 r produces this effect when a 5 cm. or larger field is used. The cancericidal dose of Wintz and Seitz, the unit skin dose of Knox and Leavitt and other English radiologists, and the therapeutic erythema dose are all second degree Holznecht reactions. This is produced by approximately 800 r when delivered in one dose provided the field is not too small. The epidermolytic dose of Regaud and Coutard is more aptly termed a $3\frac{1}{2}$ degree Holznecht, since a complete denudation of the epidermis is supposed to occur, and usually follows a single dose of about 1500 r.

Before closing the preliminary discussion of erythema we should recall the theory of erythema waves advanced by Miescher and quoted by Knox and Leavitt⁴ in their textbook. Miescher believes that x-ray erythema reactions occur in definite waves as follows:

1. An early reaction or first wave which occurs in 24 to 48 hours.
2. A second wave which appears in from 8 to 22 days.
3. The third wave in from a month to 5 weeks, and occasionally a fourth wave after 3 or 4 months.

I have not been able to find the theory of such erythema waves but Leavitt says he frequently sees the first wave and we have also observed slight erythema or swelling or both in from $\frac{1}{2}$ hour to 48 hours after exposure, with the later development of a second or third wave at more or less the usual time expected and with the degree or reaction planned.

In spite of this old and widely known information about skin reactions it is a great mystery that only in the last two or three years has the power of the skin to recover from large doses of radiation become generally accepted. All radiologists and other physicians interested in cancer realized for many years that it was in only the very occasional case that a sufficient dose could be applied to an

internal malignancy. We were always confronted with the fear of an unhealing x-ray burn and we continued to treat far-advanced cancer cases with small doses of irradiation, the dose being so small that frequently not even a first degree erythema reaction took place—and cancer patients continued to die with monotonous regularity.

The new intensive x-ray technics offer nothing new in skin reactions as the same previously described erythema changes take place with much the same doses. The novelty and effectiveness of protraction and fractionation are best demonstrated by the great ease with which the skin can recover from the alarming looking $3\frac{1}{2}$ degree Holznecht reaction. A patient will be seen, after a postoperative series of irradiation to the breast for example, with an enormous, raw exuding surface. The first time this is seen one feels certain that he has produced a hopeless x-ray burn. In about three weeks the patient will return for observation and we find that the denuded surface has completely healed with good new skin.

The evolution of the idea that the skin could stand much larger doses of x-ray began with the work of Regaud. While Regaud was using a radium pack with a low intensity of radiation (approximately 4 r per minute) he discovered that as much as 5000 r could be applied in about two weeks time. This caused a very marked reaction, that he termed epidermolysis—loss of the entire epidermis, but healing took place promptly and completely. Regaud thought this was a peculiarity of the short wave length of the radium rays plus the low intensity with which radiation was administered. However, one of his associates, Coutard, soon demonstrated that the skin could withstand just as much x-radiation when a very heavy filtration and the equivalent low intensity were employed. For a while the radiologic world then felt that the low intensity (approximately 4 r per minute) and the heavy filtration (2 to 3 mm. of copper) were the reason for this, and were necessary if irreparable burns were not to result from heavy doses. It was not long, however, before radiologists who had neither the time nor the patience to carry out a technic requiring several hours for each treatment, discovered that apparently neither the low intensity nor the extremely heavy filtration were necessary. Mattick⁵ and Harris⁶ were some of the first to discover and publish that with the generally used "deep" therapy technic (200 kvp, 0.5 mm. Cu filter and an intensity of 10 to 75 r per minute) practically the same large dosages could be delivered with very little if any more skin reaction. Mattick⁵ comes to the following conclusions from experimental work done at the State Institute for the Study of Malignant Disease of New York:

1. It is apparently optional whether we use a heavy 3 mm. copper filter or the ordinary 0.5 mm. copper filter in producing the epidermolytic reaction.
2. Protraction or diminished r per minute intensity while a safeguard is not a necessity.
3. The total r dose is of little or no clinical significance unless the duration of the treatment time in days and the cumulative or effective r dose are also given.

McWhirter⁷ in a recent article on radio-sensitivity in relation to the time-intensity factor comes to the same general conclusion as Mattick, i. e., "low intensity methods have no biological superiority over high intensity methods. Should further experiments show that a more marked erythema results from high intensity methods it will remain to be demonstrated that the damage to the tumor has not also been proportionately greater."

This is a logical place to point out that in spite of the widespread opinion that the skin will tolerate more radiation when a shorter effective beam is used and that "skin effect is determined almost entirely by the long wave lengths in the beam and the backscattering",⁸ authoritatively done experimental work does not agree with this. Schwarz and Frank⁹ from their vast experience come to exactly the opposite conclusion:

The widespread opinion that soft roentgen radiation is more damaging to the skin than the hard rays is erroneous. In similar doses, radiation is more injurious to the skin the greater the deep effect of the radiation. . . . Rays of 170 Kv. are, in ionometrically similar doses, more injurious to the skin than rays of 110 Kv. Between 110 Kv. and 60 Kv. there exists no appreciable difference in skin reactions produced by them.

Hodges, Brunschwig and Perry¹⁰, from experiments on animals and the human skin, found no difference in reaction over the voltage range from 80 Kv. to 200 Kv. and concluded "There is no reason to suppose that the situation will be different for voltages in excess of 200 Kv." My own experience agrees with Schwarz and Frank, "in similar doses, radiation is more injurious to the skin the greater the deep effect."

No attempts at figuring the exact recovery of the skin by curves or percentages have been attempted unless identical daily quantities of radiation are administered. According to MacComb and Quimby and Reisner⁸ the skin recovers approximately 50 per cent in the first 24 hours and 25 per cent daily after that through the sixth day. From the seventh day on the daily recovery drops to about 20 per cent. Although they do not give figures after the twelfth day we have considered from our own experience that the recovery is about 10 per cent daily up to 3 weeks.

We do not feel it is necessary or important to try to determine exactly the mathematical daily recovery of the skin for several reasons. First, we are certain it cannot be done accurately since unquestionably different patients vary fundamentally in their susceptibility and recovery to radiation; secondly, there are too many variations in technic and physical factors that profoundly influence skin reactions even if all patients responded exactly alike to identical dosages; and finally, many times treatment days have to be skipped because of the poor condition of the patient or for other sound reasons. In this field, by necessity, we are forced to turn back from the science to the art of medicine. We may use experiences of others as a guide but it is necessary for each of us to determine the final solution with our own apparatus and on our own patients. Fortunately, with prolonged fractionation of treatment, even as short as 10 or 12 days, we can after a little practice in careful observation of the skin frequently foretell the final reaction before it occurs. For example, if after eight daily increments of 250 or 300 r we observe a definite second degree erythema developing, this patient has had his biologic tolerance of radiation in that field and we stop the treatments to observe a gradual increase in this reaction, for about two weeks, to loss of the entire epidermis, a patchy epidermolysis, or a 3½ degree Holznecht reaction as the final result. This will heal in from three to four weeks.

A final word concerning the method of healing or epithelializing is of interest. Cameron¹¹ has studied healing following severe x-ray reactions. He considered the following possibilities:

1. Mitosis of the remaining cells of the burned region.
2. Lateral migration from nearby uninjured skin.
3. Amitosis or modified mitosis.
4. Migration and differentiation of cells of the dermis, or of deeper layers of the body.

His microscopic studies revealed there was no significant increase in mitotic divisions and there was no evidence of amitosis. He concluded that, "Traveling cells were much more numerous during the period of regeneration. These findings support the idea of replacement of epidermal by dermal cells."

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TISSUE EXTRACTS IN TUMOR THERAPY

Attempts to influence cancer by injection of tissue or organ extracts have been made periodically for a generation but the utility of such methods, alone or combined with roentgen and radium irradiation, has not been widely accepted. However, advances in biochemical knowledge have helped to dispel some of the empiricism which surrounded earlier efforts along these lines, have led to the preparation of less conglomerate extracts, and have made possible more adequate evaluation of the therapeutic potentialities of such preparations. There is an ever broadening trend to regard neoplasia and its control from a biochemical viewpoint and, in the light of our increasing information as to the importance of hormones in cancer production, it is as Shaw¹ says, "quite conceivable that their qualitative and quantitative regulation may prove to be a factor in its destruction."

The data relating to experimental and clinical use of tissue extracts in cancer therapy, even those amassed in the recent past, are too voluminous to enumerate here. Reviews by Lustig and Wachtel,² Voegtl³ and Nicholson⁴ indicate some of the suggestive evidence of the last few years. Hormone and enzyme solutions, extracts, autolysates and decomposition products of normal and cancer tissues, blood, serums and ascitic fluid have been tested on animals and used in practice in attempts to inhibit growth or cause regression of tumors. Conflicting reports are not unusual; amelioration of symptoms often results; and non-specific protein reactions have undoubtedly been obtained in many cases.

Von dem Borne⁵ reported doubtful success with Fichera autolysates of spleen, lymph glands, thymus and bone marrow. Hypodermic injections of extracts of spleen and thymus have been used because these organs rarely become cancerous, indicating perhaps that they possess some form of resistance. Blumenthal, Jacobs and Rosenberg⁶ used liver, spleen, stomach, pancreas and intestine extracts from freshly killed animals and they point out morphologic changes in the nerve cells and blood vessels of the tumors. These specific changes they believe stimulate the reticulo-endothelial system which seems to play a significant role in healing both metastases and primary tumors. Roskin and Romanowa⁷ also attributed the inhibition (of transplanted mouse carcinoma) by *Schizotrypanum cruzi* endotoxin to stimulation of the reticulo-endothelial system. With sufficiently large subcutaneous doses of concentrated extract from fresh spleen Lewisohn⁸ obtained regression of mouse sarcoma; liver, heart, pancreas and testis extracts failed to produce splenic enlargement, to cause hemorrhages into the tumor or to influence its growth.

The production of hemorrhagic lesions in tumors and the subsequent regression of some tumors can also be effected by bacterial preparations. Shear and Andervont⁹ isolated a water-soluble fraction from *B. coli* which regularly produced hemorrhage in mouse tumors in minute doses; Fogg¹⁰ obtained good results with the alcohol-insoluble fraction from various bacilli in treating transplanted mouse sarcoma and carcinoma but was unable to obtain regression of spontaneous tumors. Andervont¹¹ also noted the failure of *B. coli* filtrates to produce hemorrhage in spontaneous mammary gland carcinomas of mice, and Eisen¹² found that *B. danysz* filtrate or vaccines evoked hemorrhagic lesions in relatively few mice bearing the Ehrlich carcinoma. Proteolytic enzyme solutions such as Connell's¹³ "ensol" have been reported ineffective against mouse,^{14, 15} rat¹⁶ or rabbit¹⁷ tumors. Mention of bacterial preparations is interpolated here because it seems that administration of protein substances may cause tumor regression in some cases.

Attempts to fractionate and isolate tumor inhibiting substances from tissue extracts are beginning to yield promising results. For example, Murphy¹⁸ and coworkers have separated tumor-inhibiting and tumor-stimulating factors from various sources (placenta, embryonic skin, mammary gland, tumor tissue). Their results indicate that active normal tissues contain both inhibiting and stimulating factors; the former is associated with protein and is water-soluble (ether-insoluble), the latter is ether-soluble. Bauer et al¹⁹ found an inhibitory factor of autolyzed spleen in the benzene-soluble portion of the alcohol extract. Helmer²⁰ extracted an agent from the

unsaturated fatty acid fraction of pancreas which inhibited chicken sarcoma and Helmer and Clowes²¹ subsequently found that various free fatty acids and soaps exert protective effects when mixed with the agent in advance.

The objective of disease treatment by imitating natural methods of cure draws nearer with each advance in the study of the body's methods of defense. Extension of information as to the properties, functions and relationships of the hormones has led to numerous efforts to treat cancer by means of these "chemical messengers". Cramer and Horning²² suggest that the thyrotropic hormone of the pituitary gland may be useful as a physiologic antagonist in treating cystic disease of the breast and benign enlargement of the prostate since these conditions are supposedly due to estrogenic hormone imbalance. Coffey and Humber²³ reported successful treatment of many patients with repeated injections of aqueous extracts of the adrenal cortex, but others have been unable to duplicate their results. From among the many trials of numerous hormone preparations tested on animal tumors, it has been reported that insulin^{24, 25} is effective against rat and rabbit sarcoma, that thyroxine²⁶ may control tumor growth by retarding dedifferentiation, and that pineal hormone²⁷ inhibits the growth of inoculated tumors in mice.

The surgeons' five or ten year standard for judging results is seldom adopted in evaluating chemotherapy of cancer and the critical attitude toward new medical treatments has resulted from the too frequent failure to maintain initial temporary improvement. The question of how to stimulate effectively a repressive activity of the organism in order to control tumors and prevent metastases is still open.

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